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ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND  
RELATED MATTERS.

Hearing held  
8th floor  
180 Dundas Street West  
Toronto, Ontario

HA STREETEN  
Hunt (cont'd)

The Honourable Mr. Justice S.G.M. Grange  
P.S.A. Lamek, Q.C.  
E.A. Cronk  
Thomas Millar

Young  
Brown

Commissioner  
Counsel  
Associate Counsel  
Administrator

Transcript of evidence  
for

December 8, 1983

For the  
The Inquiry

VOLUME 78

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ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
DEATHS AT THE HOSPITAL FOR SICK CHILDREN  
AND RELATED MATTERS.

Hearing held on the 8th Floor,  
180 Dundas Street West, Toronto,  
Ontario, on Thursday, the 8th day  
of December, 1983.

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner  
THOMAS MILLAR - Administrator  
MURRAY R. ELLIOT - Registrar

APPEARANCES:

P.S.A. LAMEK, Q.C. ) Commission Counsel  
E. CRONK )  
T.C. MARSHALL, Q.C. ) Counsel for the Attorney  
D. HUNT ) General and Solicitor General  
L. CECCHETTO ) of Ontario (Crown Attorneys  
and Coroner's Office)  
I.G. SCOTT, Q.C. ) Counsel for The Hospital for  
M. THOMSON ) Sick Children  
R. BATTY )  
D. YOUNG Counsel for The Metropolitan  
Toronto Police  
W.N. ORTVED Counsel for numerous Doctors  
at The Hospital for Sick  
Children  
E. MCINTYRE Counsel for the Registered  
Nurses' Association of Ontario  
and 35 Registered Nurses at  
The Hospital for Sick Children







APPEARANCES (Continued):

D. BROWN	Counsel for Susan Nelles - Nurse
E. FORSTER	Counsel for Phyllis Trayner - Nurse
J.A. OLAH	Counsel for Janet Brownless - R.N.A.
B. JACKMAN	Counsel for Mrs. M. Christie - R.N.A.
S. LABOW	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, Mr. Mrs. Lutes, and Mr. & Mrs. Murphy (parents of deceased children)
F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo); and Heather Dawson (mother of deceased child Amber Dawson)
W.W. TOBIAS	Counsel for Mr. & Mrs. Hines (Parents of deceased child Jordan Hines)
J. SHINEHOFT	Counsel for Lorie Pacsai and Kevin Garnet (parents of deceased child Kevin Pacsai).






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TORONTO, ONTARIO

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BmB.jc

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--- Upon commencing at 10:00 a.m.

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THE COMMISSIONER: Before I forget

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I have very short matters on elsewhere on Monday

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and Wednesday of next week at 10 o'clock. So, we

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won't sit until 10:30 on both Monday and Wednesday.

7

Yes, Mr. Hunt?

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MR. HUNT: Thank you.

9

DR. ALOIS RUDOLF HASTREITER, Resumed

10

MR. HUNT: Good morning, Doctor.

11

THE WITNESS: Good morning.

12

EXAMINATION BY MR. HUNT (CONTINUED):

13

Q Yesterday at the close of

14

Mr. Lamek's examination he asked you about the lesson

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to be learned from the Gary Murphy case and at page

16

6946 of Volume 77, I will just read you the question

17

and answer. The question was:

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"I guess the thing upon which I

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invite your agreement is this; that

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the lesson of Gary Murphy is that we

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have to be cautious in looking at any

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particular case from the epidemic

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period where there is not clear

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toxicological evidence, lest we too

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easily be suspicious on insufficient

grounds, is that fair, would you agree

with that?





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"A. Could you repeat that, please?

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"Q. Yes, we have got to be cautious

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in looking at any particular case

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where there is no clear toxicological

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evidence, cautious lest we be too

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easily suspicious on insufficient

8

grounds?

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"A. I think that is a correct

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observation."

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Now, I just invite your comments, sir,

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on something that Dr. Phillips said to us when he

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testified here on November 1st, and this is in

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Volume 59, Mr. Commissioner. It is at page 3102. As

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you know, Dr. Hastreiter, Dr. Phillips is the Chief

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of Pathology at The Hospital for Sick Children. At

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line 16 and following these questions and answers

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were asked:

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"Q. Would it be fair to categorize

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this study into post mortem digoxin

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data ... "

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I should indicate he was referring to the study that

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was undertaken at the Hospital after March of '81

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where levels were taken on all children that died.

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A. Yes.

Q. "Q. Would it be fair to







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"categorize this study into post mortem digoxin data involving now, I suppose, over 608 samples as perhaps the most extensive one ever conducted anywhere into digoxin?

"A. I think so, yes.

"Q. There is no study that you are aware of anywhere in the world that has that large a sample to work from. Is that fair?

"A. That is correct.

"Q. That being the case, you said yesterday that the levels such as the level in Justin Cook and perhaps some of the others such as Inwood and Pacsai, with the exception of the Gary Murphy case, have never been repeated in this study?

"A. That is right.

"Q. So that the events, whatever the combination of events were that led to what happened in March of 1981, and I am referring to the consecutive deaths at the levels that were reported in Inwood and Hines and Pacsai





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"and Miller and Cook, that has never repeated itself in the course of these 600 or 700-odd cases that have been examined?

"A. That is correct.

"Q. I suggest, sir, that if the events that gave rise to what happened in March of 1981 had been a natural medical phenomena would we not have expected to see some sign of that in the course of the research that has been done?

"A. I think so, that by now we probably would be expecting to have found some elevated values in those ranges.

"Q. And the fact that we have not seen a repeat of the factors, the combination of factors that gave rise to the events of March as this study has progressed and progresses, I take it makes it less likely that the events of March of 1981 were simply a natural medical phenomena?

"A. I think that is correct."







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Would you agree or disagree with  
Dr. Phillips' comments?

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A. I agree with him.

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MR. HUNT: All right. Thank you, sir,  
those are all the questions I have.

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THE COMMISSIONER: Thank you. Mr.  
Young?

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MR. YOUNG: Thank you, Mr. Commissioner.

9

EXAMINATION BY MR. YOUNG:

10

Q. Good morning, Doctor.

11

A. Good morning.

12

13

Q. Doctor, my name is David Young  
and I'm representing The Metropolitan Toronto Police  
at these proceedings.

14

15

In reviewing your CV, Doctor, Mr. Lamek  
mentioned to you that it is indicated you were the  
Director of Paediatric Cardiology at the University  
of Illinois Hospital. I understand you held that  
post until some time last year?

16

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18

19

A. Right.

20

21

Q. Did you retire at that time, is  
that what happened? Why are you no longer involved  
in that program?

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A. No, I am doing more private  
practice and it would have been difficult for me to





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stay as Director of the section and do private practice.

Q And is the University of Illinois Hospital a teaching hospital, Doctor?

A. Yes.

Q Doctor, you continue to be a Professor of Paediatrics, do you not, at the University of Illinois?

A. Yes.

Q Could you describe for us just what that job entails, how much of your time is spent teaching and if any of your time is spent in research, how much of your time is spent doing that?

A. I would say that I spend about 40 per cent of my time seeing patients, doing clinical patient care, 30 per cent in research and then maybe 20 per cent teaching, or, let's say 15 per cent teaching, 15 per cent administration, something like that.

Q As we learned yesterday you have done a great deal of research into digoxin and its effects on infants and neonates and children generally. I notice in going through your CV that there are over 20 articles or research projects listed there and you mentioned to Mr. Hunt that there are probably







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a few that aren't listed in the CV?

A. That is correct.

Q. The ones listed in the CV include "Disposition of Digoxin in Pre-term and Term Neonates", "Drug Overdose and the Heart", "Digoxin Tolerance in Infants", "Post Mortem Digoxin Concentration in Infants", and it goes on and on, in all topics that are quite relevant to the study that we are conducting in these proceedings, would you not agree?

A. I believe so.

Q. Yes. Now, Doctor, if we could move forward to May of 1981. That is I believe when you conducted your first review of the medical records of the children that we are concerned with.

A. Right.

Q. I think you told the Commissioner that you spent two days doing that initially, is that correct?

A. I don't exactly remember. I believe there were two days because I came several times. Sometimes I spent one day and I think once I spent two days.

Q. Doctor, we have spent a good





A.8

1  
2 deal of time talking about the Estrella chart, or  
3 the Estrella infant and particularly the 72 level  
4 that is listed in the chart. Mr. Lamek asked you  
5 some questions about that and yesterday Mr. Hunt  
6 asked you some questions. I'm not going to spend a  
7 long time on the matter but I have a few other points  
8 that I would like to bring up with you. If we could  
9 just talk about -- first of all, we heard Dr. Taylor's  
10 evidence yesterday. Both Mr. Hunt put his evidence  
11 at the preliminary to you and he also put the  
12 evidence that we heard in these proceedings from  
13 Dr. Taylor to you, talking about the manner in which  
14 he took the sample and possible contamination and,  
15 more particularly, he recently told us during these  
16 proceedings about possible fecal contamination.

17 We also heard Dr. Mancer's evidence  
18 at the preliminary hearing where he stated that the  
19 level of 72 is, if anything, artificially low but  
20 not likely high. Do you recall that, Doctor?

21 A. Yes. If it were contaminated  
22 by ascitic fluid or edema fluid, that is what one  
23 would expect. However, if it were contaminated by  
24 fecal material or gastric or intestinal contents it  
25 could be the other way.

Q. Right. But of course at the





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preliminary there was no mention of possible fecal contamination?

A. No, there was not, right.

Q And finally, some of Mr. Cimbura's comments with respect to the gutter blood study were also put to you yesterday.

A. Right.

Q This particular gutter blood study, Doctor, my understanding is that it was a co-operative venture, so to speak, between the Hospital and the Centre of Forensic Sciences and one of the individuals at the Hospital that was quite involved was Dr. Phillips and you have already heard some of his evidence today. Dr. Phillips is the Head of Pathology and Dr. Phillips didn't testify at the preliminary hearing but he did testify in these proceedings. I wonder if I might just read to you some of his evidence and ask you to comment on it?

This is in Volume 58, page 2993. The question is put by Miss Cronk:

"Q Doctor, we know and of course you are aware that the gutter blood specimens drawn from the body of Janice Estrella resulted in a reading on post mortem assay conducted at







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And here's his answer, Doctor:

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"the Hospital of 72 nanograms per millilitre. In light of the gutter blood study and the data which was provided to you as a result of the assays conducted on those 14 cases, how would you as a pathologist regard that level of 72 nanograms in the case of Janice Estrella?"

"A. Well, it is a difficult question. After considering it in considerable detail I thought that it probably served to muddy the issue a bit. Because I must say my own personal view was that a gutter sample was probably a reasonably accurate record, would probably be similar to the blood, I was actually surprised at these results here, that the gutter fluid specimens can be so different or whatever, that is the way I thought of it."

And later Dr. Phillips told us during questioning by Mr. Olah, and I am on page 3122 of Volume 59 now. Mr. Olah asks:





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"Q. I guess what we need from you, Doctor, is assistance in terms of your expertise as to the kind of confidence that we should place upon a reading of that kind. Are you suggesting then that in fact gutter blood samples should rank below tissue samples in terms of their reliability, or is it something that is more reliable than that?"

And his answer was:

"A. Well, this particular type of sample obtained from the pelvic gutter which is potentially contaminated by material from the bowel, no matter what measures you take to try and prevent it it is always possible, because one has to cut across the bowel. Even if you tie and this sort of thing there is still the possibility of that happening I really think that is far from an ideal sample."

And he goes on to say:

"I must be quite fair and honest with you about this, that when we got





1  
2 "this value back we thought it was  
3 signifcant, and it was only after we  
4 did the study and sorted of looked  
5 at it closer to see exactly what kind  
6 of sample it was and the potential  
7 for contamination of it that we sort  
8 of had more concerns about it."

9 It seems Dr. Phillip believed, as  
10 Dr. Mancer did, that that was in fact, the level  
11 of 72 was in fact a valid reading, the true reading;  
12 is that your understanding of the evidence I have  
13 just put to you, Doctor?

2  
14 A. My understanding is that  
15 initially we thought so and that later he developed  
16 some doubts about it.

17 Q. That is correct, Doctor, and  
18 it was only after the gutter blood study was  
19 completed that these doubts developed?

20 A. That is correct.

21 Q. And I wouldn't imagine that  
22 would surprise you, Doctor, because it is my  
23 understanding that the prevailing medical opinion  
24 at the time of the preliminary hearing, and in fact  
25 up to the conclusion of the gutter blood study,  
was that the level of 72 on Baby Estrella was in







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2 fact a true reading, an accurate reading. If  
3 it was not, it was likely artificially low; is  
4 that your understanding?

3  
5 A. That is my understanding, yes.

6 Q. Doctor, let's move forward  
7 to the second phase of this Police Investigation;  
8 and you were also involved in a number of meetings  
9 that were held. One of them was held on August  
10 27th, 1982, and another was held on September 13th,  
11 1982. We have copies of all portions of those  
12 minutes marked as exhibits in these proceedings;  
13 and I would like to refer you to Exhibit 269.

14 Mr. Commissioner, that is the  
15 expurgated notes of the minutes of the August  
16 27th, 1982 meeting.

17 If you would look towards the bottom  
18 of the second page of those minutes, Doctor, there  
19 is a quote that is attributed to you, and it says:

20 "Dr. Hastreiter said that there had  
21 been one child who accidentally died  
22 following intravenous level of 200."

23 Do you see that, Doctor?

24 MR. ORTVED: I am sorry, what exhibit?

25 MR. YOUNG: I am sorry, Exhibit 269.

THE WITNESS: Page 2 you say?





1

2

Q. The second page, yes.

3

A. The second page, oh, yes.

4

Q. It is the very last sentence.

5

A. Yes, the very end.

6

Q. And I suggest to you, Doctor,

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that you were referring to a case that was reported

8

in the literature and not one of the children that

9

we are considering in this inquiry when you made

10

that comment, is that correct?

A. That is correct.

11

Q. If we could move forward a

12

little further then, Doctor, to that September

13

13th meeting; do you remember how long that meeting  
lasted?

14

A. I didn't remember until I

15

looked at the Minutes, and it says here it lasted

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about seven hours, from 10 in the morning till 5

17

in the evening, I believe there may have been a

18

lunch break, I am not sure.

19

Q. That seems reasonable.

20

Doctor, on these Minutes, our Exhibit 261, at page

21

1 in the second last paragraph on the page, there

22

is a quote attributed to Staff Sergeant Press.

A. Yes.

23

Q. That he describes the format

24

25





1  
2 of the meeting and he goes on to say, or the minutes  
3 state:

4 "Staff Sergeant Press advised that the  
5 format of the meeting would be for  
6 Dr. Hastreiter to give an opinion on  
7 each chart, followed by Dr. Fay,  
8 Mr. Cimbura, Dr. Gilmour-Bryson, Staff  
9 Sergeant J. Wolfe and Sergeant Lowe  
10 (who examined nurses' statements),  
11 and Staff Sergeant Press (who examined  
12 doctors' statements). Opinions would  
13 then be offered for the group to reach  
14 agreement on the category on which  
15 each death would fall. Staff Sergeant  
16 Press advised that, wherever possible,  
17 investigators would visit parents to  
18 advise findings, concerning their  
19 children."

20 And then if we turn, Doctor, to page  
21 6 of the same Minutes, there is another quote  
22 attributed to Staff Sergeant Press right at the  
23 very top of the page it says:

24 "Staff Sergeant Press expressed the  
25 need to present a united front."

And I will refer you to one other







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passage, Doctor, on this same page, page 6, there

3

is a comment:

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"Mr. Wiley advised that this decision  
should not be looked at from the point  
of view --"

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THE COMMISSIONER: I am sorry, where  
is that?

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MR. YOUNG: I am sorry, Mr. Commissioner,  
we are on page 6.

10

11

THE COMMISSIONER: Yes, I am on page  
6.

12

13

MR. YOUNG: It is about the eighth  
line, the seventh line down.

14

THE COMMISSIONER: Oh yes, yes, all  
right.

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MR. YOUNG:

"Mr. Wiley advised that this decision  
should not be looked at from the point  
of view of proving cause of death and  
going to court; this is to come to some  
conclusion to discuss with parents."

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Now, Doctor, based upon these passages  
from Exhibit 261, I would suggest to you that the  
purpose of the September 13th meeting was to reach  
a consensus as to the cause of death of these children





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where possible so that some of the parents could be finally given an answer as to how their children died, as to whether or not their children were murdered, is that your recollection, Doctor?

A. That is my recollection that this was the main function of that meeting.

Q. And, Doctor, I understand that at that meeting some evidence was presented, some facts were presented that indicated that there was a similarity of the terminal events of some of these children, do you recall that?

A. Yes.

Q. There was also some information presented that indicated that certain nurses were present when these children died; do you remember that?

A. Yes.

Q. And did you consider this information in reaching your conclusion as to the cause of death?

A. No, I didn't.

Q. And at this meeting we have heard evidence from Dr. Fay that Mr. Cimbura, yourself and Dr. Fay did most of the talking at the meeting; and for my friends that is Volume 68,





1  
2 page 4968, is that your recollection of how the  
3 meeting proceeded?

4 A. Yes.

5 Q. If we could look at that  
6 same page of Volume 68, that is page 4968; Dr.  
7 Fay describes a number of occurrences at the meeting,  
8 the bottom of page 4968, that is line 18 and he  
9 says:

10 "Q. Certainly. And they came into  
11 the meeting with, in some cases,  
12 different opinions, different views,  
13 different interpretations?"

14 That was a question from me; and the answer was:

15 "A. Well, I think that was the purpose  
16 of the meeting. I mean, after all,  
17 if that hadn't been the purpose of  
18 the meeting, I suppose we could have  
19 just submitted a written report and  
20 let somebody go through it in a  
21 clerical fashion and construct the  
22 opinion from that."

23 Doctor, do you recall that as being  
24 one of the purposes of the meeting?

25 A. Yes.

Q. For instance, Doctor, in the







1  
2 case of Baby Inwood, after the first vote, a  
3 second discussion was held, and you told us the  
4 other day that you altered your opinion as a result  
5 of this subsequent discussion and specifically  
6 comments made by Mr. Cimbura about the toxicological  
7 evidence; do I have that right?

8 A. Yes.

9 Q. And I suggest to you, Doctor,  
10 that the minutes don't reflect any comments that  
11 Mr. Cimbura made during that second discussion,  
12 would you agree?

13 A. I agree with that.

14 Q. Before I sit down, Doctor,  
15 and let someone else ask you a few questions,  
16 there is two other matters I would like to raise  
17 with you, and this is just to keep the record  
18 clear.

19 The first is that comment at the top  
20 of page 6 of Exhibit 261, the comment attributed  
21 to Staff Sergeant Press where he is said to have  
22 noted the need to present a united front, did that  
23 particular comment, Doctor, convince you to change  
24 your vote with respect to Baby Inwood?

25 A. No, not at all.

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A. No, not at all, but as you indicated earlier the main function of this meeting was to reach an agreement or some type of conclusion about the death of these children which would be a consensus of opinion of everybody involved because everybody had knowledge of different aspects of the case and we just wanted to bring it all together and reach a final consensus opinion.

Q. My last question to you is this: Did any of the police officers, Crown attorneys, Coroners, attempt to induce you, coerce you or influence you in any way, shape or form to change your opinion during the September 13th meeting, before or at that meeting?

A. Never.

MR. YOUNG: Thank you very much, doctor.

THE COMMISSIONER: Thank you.

Mr. Brown?

CROSS-EXAMINATION BY MR. BROWN:

Q. Dr. Hastreiter, my name is Brown. I act for Susan Nelles.

One of the aspects of your testimony which I think is probably of great significance were your efforts to try and ascertain of a certain number





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of babies when what is described as digoxin was administered to the child, the possible route of administration and the time of administration.

I understand when you were initially retained in this matter and asked to look at a number of medical records there were really two things that you were asked to do: the first was in a general way to ascertain whether or not digoxin may have been involved in the deaths of the children you were reviewing. I take it that was one of the purposes of your chart review?

A. Yes.

Q. And I take it a second purpose was that in certain cases where you thought there was sufficient evidence you would attempt to give an estimate on the possible time that digoxin was administered, on the possible route and the possible dose. Was that sort of the second part of your review?

A. Yes.

Q. Now the involvement of digoxin in the deaths of the children from what I gather you really looked at the clinical evidence as disclosed by the medical records to form your opinion; is that correct?





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A. Yes. Clinical and laboratory evidence that was available.

Q. That is right. And then in the second part of your enquiry where you were trying to ascertain where possible the time, route and dose of administration, you would have to rely not only on the clinical information that you saw but also on the toxicological data so you could make certain pharmacological assumptions and therefore arrive at your conclusion.

Would that be a fair statement of the way you proceeded?

A. That is correct.

Q. Now when we are interested in trying to find out the time and the route and the dose of the administration of a drug, there are a number of variables that we have to consider in that equation, aren't there?

A. Yes.

Q. We are in some cases given the concentration, and we need to know that. Another factor would be the time of administration. Another factor would be the dose administered.

I take it that with those three factors, if you had any two of those factors, let us







1  
C4 2 say the concentration of the sample, and you know  
3 when the sample was taken and you know the dose that  
4 was administered, you could fairly reasonably estimate  
5 when the dose was administered?

6 Would that be a fact?

7 A. That is correct. I think you  
8 did not mention the route of administration which is  
9 also important.

10 Q. The route of administration,  
11 so that would also be a fourth factor in the equation?

12 A. Yes.

13 Q. So if one was to know, let us  
14 say, three of the four factors, the time of administra-  
15 tion, the route of administration and the dose, one  
16 could make a fairly safe estimate as to the expected  
17 concentration at a particular point in time, could one  
18 not?

19 A. That is correct.

20 Q. But of course as soon as you  
21 start eliminating a number of the variables, that is  
22 if you don't know the time of administration and you  
23 don't know the dose that was administered, and you  
24 only know the route and concentration of it, it becomes  
25 more difficult to ascertain with any degree of  
certainty one of the unknown variables, isn't it?





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A. That is correct.

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Q. And so of course if one only

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knows one out of the four variables, that is the concentration, it becomes even that much more difficult to try and determine any of the other three variables, the time of administration, the dose administered and the route of administration? Wouldn't that be fair?

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A. That is fair.

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I think one would have to make certain assumptions. For instance, when you are dealing with a very high level it would be unlikely that a child would live with a level as high as this for a long period of time, so that would be something that must be taken into consideration.

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It would also be difficult to achieve such a level, for instance, given an oral administration, in some cases perhaps, and that should be taken into consideration, so this is how one could narrow things down as well as possible, but the margin of error is still considerable.

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Q. Well, that is perfectly fair.

Of course as you say you have to make certain assumptions. If you only know one of four variables, you have to make reasonable assumptions about some of the other three?





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A. Right.

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Q. In order to arrive at an

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answer?

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A. Right.

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Q. And the estimate is only as

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good as the assumptions, and if there is an error in  
the assumptions, there could be an error in the

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conclusion? That is one of the inherent difficulties  
in this sort of exercise, isn't it?

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A. Certainly. One has to be

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very careful with the assumptions that are made.

12

Q. Precisely, and as I think you

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have said even if you do make the best assumptions

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possible in this sort of exercise, there is still the  
possibility of a margin of error, is there not?

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A. There is.

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Q. And one cannot really tell

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with any degree of certainty, knowing only the

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concentration found at a particular point of time,

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what any of the other three variables are? One can  
only suggest a possibility, can one not?

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A. I would go a little further

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and say that there are -- it is a matter of probabilities

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really, and one would try and weigh one situation

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against the other and try to determine which one would

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be more likely and give it a certain rating or grading, and this way narrow down the situation as well as possible. But there is a considerable amount of variability and there is an error involved.

Q. And so would I be fair in saying that whatever estimate you come up with, this is certainly the best estimate you can make operating under certain assumptions, but having all due regard to the inherent difficulties in this sort of exercise, the estimates that you make are not fixed in stone? They too are subject to possible error and variation, are they not?

A. Definitely.

Q. And in view of the inherent difficulties in this sort of exercise, it would not be surprising, would it, to find that when other experts apply their minds to these problems, the answers that they arrive at are not necessarily the same as yours?

A. Yes.

Q. And indeed in view of the difficulties in this exercise one would expect that sort of variation in opinion, would one not?

A. To some degree.

Q. Well, I agree completely it







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would be a matter of degree, so we have heard from several pharmacologists before us that their estimates as to the range for time of administration might be slightly different in degree than yours.

For example, Dr. Spielberg was here and when asked in respect to Baby Justin Cook when he thought the most likely time was that the digoxin was administered, he initially said sometime between 3:45 in the morning, which you may recall was the time of this episode, and 4:20, the time of the arrest. And under further questioning he said he might consider that period shortly before 3:45. So the opinion he reached is not identical to yours, is it?

A. No, it is a little bit different. I think I said half an hour before. Half an hour to an hour before 3:45. Perhaps we should refer back to what I said. I don't remember the times exactly now.





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Q. Well, if I recall, and my

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friends can correct me, you thought that your best

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estimate was somewhere between 3:15 and 3:40 in

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the morning, which would be about 25 to 30 minutes

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before what you thought were the onset of the

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terminal events?

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A. Right. So, his estimate was a

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little shorter than mine, but the difference is not

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Q. Is not that great. Well,

11

it would be another possible estimate as to the

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time of administration of that drug but it is within

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the realm of possibility, is it not?

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A. Yes.

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Q. And in view of the difficulties

16

inherent in that exercise that may well be the time

17

at which the drug was administered, could it not?

18

A. Could have been. It would

19

have been difficult to explain why the child had

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this one episode and never recovered from it.

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Q. Well, we will deal with that

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in a minute.

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A. Yes.

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Q. We heard from another

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pharmacologist from the Hospital, Dr. MacLeod,





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and when he was asked the same sort of question about Justin Cook he said that in his opinion he thought that the digoxin was administered again some time between 3:45 and 4:20 in the morning. He was asked whether he would push it back any earlier than that, before 3:45 and he said he had some difficulty with that because ---

MR. LAMEK: Excuse me, Mr.

Commissioner. Would Mr. Brown be good enough to read that evidence for me.

THE COMMISSIONER: Yes.

MR. LAMEK: It is not my recollection of it.

THE COMMISSIONER: Yes.

MR. BROWN: Very well.

Q. Dr. MacLeod is testifying here, one of the days was November 9th and his testimony is found at Volume 63, starting at page 4194, line 20. He was asked this question:

"Q. Does that then take us to one of two possibilities, Doctor; that is, either that digoxin was administered ---"

THE COMMISSIONER: Is that Mr. Lamek's examination?





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MR. BROWN: Yes, Mr. Commissioner,  
it was.

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THE COMMISSIONER: Yes, all right.

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MR. BROWN: Q.

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"that is, either that digoxin was  
administered prior to 3:45 - perhaps  
again accidentally, and we may have  
to explore the possible occasion -  
or after 3:45 but perhaps not  
accidental? Are those the options  
to which we are driven?

A. Yes. Well, I am sorry, can  
we take them one at a time.

Q. Yes.

A. Prior to 3:45?

Q. Prior to 3:45 is one possible  
time for the administration of  
digoxin?

A. Yes.

Q. Now, do you regard that as  
likely? Do you, as a pharmacologist,  
regard that as likely?

A. No, I find that very unlikely,  
because you are getting too far out  
on this alpha distribution phase;







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"so then you are into the multiple  
vial and large volumes, or relatively  
large volumes. I find that unlikely.

Q. Do I therefore understand you  
that your likely time frame for the  
administration of the drug is between  
3:45 and 4:25?

A. Yes, that is correct."

Now, Dr. MacLeod was also questioned  
the following day on November the 10th, and this  
is found in Volume 64 at page 4394 and again, about  
the possible time of administration of digoxin to  
Baby Cook.

THE COMMISSIONER: By whom, Mr.  
Brown?

MR. BROWN: This is by Mr. Hunt, Mr.  
Commissioner.

THE COMMISSIONER: Yes.

MR. BROWN: Q. The question started  
at the top of page 4394:

"Q. We will have to I suppose  
look at the question of what happened  
before 3:45 at some other point;  
but in terms of what we see here as  
the baby's distress beginning at









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"3:45, are you satisfied that that is as consistent with the beginning of the effects of digoxin taking place as with anything else that we have heard?

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A. Well, no. I think I have told you repeatedly that that is more consistent with the natural cause of this child's heart disease, and that it is likely whatever sequence of events is attributable to digoxin begins some time after that. The manifestations of digoxin toxicity are so vague that almost anything can happen. So, I can't say it is incompatible at all. You know, I surely don't want to be that dogmatic. I think if you move back much before 3:45 you are then going to have to postulate multiple vials, and that is possible too."

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Perhaps I can summarize that by saying that ---

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MR. HUNT: Well, there is one more very important passage that I was sure my friend





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2 was going to get to but he has closed his book,  
3 so, I rise. If he just continues over to page  
4 3496, the question that begins at the top of that  
5 page is where I put to him precisely what Dr.  
6 Spielberg said about the time being 3:45 to 4:20  
or shortly before. I then asked him:

7 "Now do you have any serious dis-  
8 agreement with what he has said  
9 there?"

10 And he said:

11 "A. No, not really any."

12 MR. BROWN: Well, Mr. Hunt anticipates  
13 the question that I was going to put to you.

14 As I said, in fairly summarizing  
15 Dr. MacLeod's evidence, Doctor, it appears that  
16 he is very similar in his view to that of Dr.  
17 Spielberg, is he not, that the time of administration  
18 of digoxin could be some time between 3:45 and  
19 the arrest at 4:20 or slightly before 3:45. I  
20 take it that would be your understanding of the  
testimony that Dr. MacLeod gave to us here?

21 A. Yes.

22 Q. So, again, we are involved  
23 in a time period which is not identical to yours  
24 and indeed part of it may be occurring at a later  
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portion of time than that which you posited, but

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I understand that you would consider that to be

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a possibility?

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A. Well, I certainly would have

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to consider it to be a possibility but I find it

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difficult to explain the high tissue concentrations

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if you make the time of the administration of the

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drug very, very short. So, there must have been

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some distribution because the myocardial level was

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Q. Well, we have heard again

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from a third pharmacologist, Dr. Kauffman, who

13

testified here last week.

14

A. Right.

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Q. And perhaps if my friends

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wish me to read that evidence. Dr. Kauffman

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was asked the same sort of question about Justin

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Cook and that appears in Volume 71, page 5564,

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and this was in his examination in chief by Miss

Cronk. He was talking here about the blood sample.

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The question started off:

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"Q. All right. And in the face,

22

Doctor, of the fact or the information

now that that sample ..."

23

referring to the blood sample:

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2 "...was taken at 4:30 in the morning,  
3 and I should say, sir, that that is  
4 reflected in the requisition form  
5 that was completed on the ward, which  
6 is part of Exhibit 32A at Tab 36.  
7 In recognition, Doctor, that the  
8 sample was taken at 4:30 in the morn-  
9 ing, does that then place the most  
10 likely time of administration in your  
11 view some time between 1:30 and 3:30  
12 a.m. on March 21st?

13 A. In those terms, yes, it would."

14 And I believe Dr. Kauffman was then  
15 asked again a number of questions about the tissue  
16 level but it was my understanding of his evidence  
17 that after being faced with the high concentrations  
18 in the myocardial tissue he retained his opinion  
19 that in his estimate the most likely time of  
20 administration was some time between 1:30 in the  
21 morning and 3:30 in the morning.

22 Now, again, that is a period of time  
23 which is slightly different than yours, is it not,  
24 Dr. Hastretier?

25 A. It is - of course, it has  
a wide range, it incorporates my time.





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Q. Yes.

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A. I would object a little to the very early timing because I find it very difficult for a child to live with extremely high blood levels such as was documented in this baby pre mortem. So, that is an accurate analysis.

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THE COMMISSIONER: You say, Doctor, my notes for what it is worth is that earlier than that he thinks that the dose was administered more than one hour before death but not much more, which would take him pretty well into precisely the time that you have?

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THE WITNESS: That I have, yes, that I had indicated. Of course, that is not what he read to me just now.

THE COMMISSIONER: And he also said that, and the reasons he thinks are because of the tissue concentration and the fact that the infant did not die earlier, it seems to be almost exactly what you have been saying?

THE WITNESS: Yes.

THE COMMISSIONER: So that while there may be some differences there also seems to be some similarity?

MR. BROWN: Some similarity. That





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indeed is the case with all pharmacologists who have testified here, there is some difference with your time frame and yet there is also some similarity with your time frame, is there not?

A. Yes.

Q. There is an overlap?

A. Right.

Q. So, the problem I have is, Doctor, that really in view of the inherent difficulties in this exercise and the overlap in times which the different experts have suggested as the possible times of administration, are we really able to do much more than to suggest, Doctor, a rather broad range of time in which the digoxin was possibly administered?

A. I don't think it is that broad. I think if you look at the various testimonies, various evidence from the various experts that, yes, some will tend to make it a little earlier and some will tend to make it a little later but there will be sort of an intermediate period where everybody more or less agrees on it, and this is the most likely time that the administration I believe would have occurred.

Q. Well, we have really then







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2 set the extremes. The outer extreme was the portion  
3 of Dr. Kauffman that I read to you which is perhaps  
4 1:30 and at the extreme closest to death would  
5 really be very close to the time of arrest. So,  
6 those would be the extreme times, would they not?

7 A. That is correct.

8 Q. And that the answer probably  
9 lies somewhere in the middle between the two of  
10 them?

11 A. Right.

12 Q. Indeed, there may be areas  
13 which you consider more likely than others, are  
14 there not?

15 A. I think all of us considered  
16 it because all of us covered that particular portion,  
17 time period as a probability.

18 Q. As a probability. But in  
19 view of the lack of knowledge as to the actual time  
20 of administration and as to the actual dose and as  
21 to the actual route, although it may in your  
22 opinion be a probability there is no way that you  
23 would see it as a certainty, would you?

24 A. I don't think in medical  
25 sciences there is anything that is a certainty,  
really. I think you can approach certainty but





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you always deal with probabilities, or almost  
always.

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Q. Now, one of the assumptions  
I believe that underlies your estimate for the  
time of administration is the nature of the event  
that took place at 3:45 in the morning. Now,  
perhaps you might want to refer to the medical  
record of Justin Cook, or you may well have the  
facts so well engraved in your mind and it is not  
necessary.

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But as you will recall, the child  
became extremely cyanotic at 3:45 in the morning,  
did he not?

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A. Yes.

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Q. And indeed at that point of  
time the doctors administer propranolol to the  
child in order to attempt to alleviate that situation.  
I take it that you are also familiar, Doctor, and  
you certainly testified to that, as to the general  
condition of this child, a child who was character-  
ized by cyanosis, and I believe that you recall  
that the previous evening at around 6 o'clock there  
was a serious cyanotic spell and at that point in  
time Inderal was administered to the child with  
apparently good effect.





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You recall that particular incident?

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A. Yes I do, that is correct.

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Q. And in view of the nature of that incident, you were present during most of the preliminary inquiry and although we haven't had it in direct evidence here, I understand that one of the doctors looking after the child ordered a vial or a syringe of propranolol be drawn up and taped to the end of the bed in anticipation that a similar problem might re-occur at a later time.

Do you recall that sequence of events?

A. Yes, I do.

Q. So, would that not suggest to you, Doctor, that in view of the event that occurred at 6 o'clock the previous evening, the doctors in charge were anticipating a repeat of that event?

A. Certainly.

Q. And indeed something did happen at 3:45 in the morning. Would you agree with me that it is quite possible that the event at 3:45 in the morning was a manifestation of the child's clinical state, it was another cyanotic spell?





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A. It is quite possible. That was the original opinion I think of everybody involved in the case.

Q. That is correct. So, it is quite possible that that was a cyanotic spell but I take it from your evidence you are of the opinion that that may well have been the onset, the manifestation of digoxin intoxication?

A. That is correct.

Q. So, we are really left with one particular event which could reasonably be the subject of two possible interpretations: a cyanotic spell or the onset of digoxin intoxication, would that be fair?

A. Yes. I think this particular event could have these two interpretations, yes.

Q. And indeed it had the interpretation that it was a manifestation of the child's clinical state and a cyanotic event, then the administration of digoxin could have occurred some time prior to then or possibly some time after that event, could it not?

A. Yes, except that as I indicated earlier I would have little difficulty explaining the very high myocardial level. You







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have to give it enough time for distribution in  
order to explain these levels.

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Q But as far as the clinical events that occurred at 3:45 are concerned, as an indicator of digoxin intoxication, would you agree with me that they are ambiguous?

A. The clinical events per se are ambiguous.

Q So in order to take those events as one assumption of the time of administration, that is that the digoxin intoxication began to manifest itself at that time, that is a possible interpretation but there is also an equally valid interpretation that that was simply a cyanotic spell?

A. That is a possibility, certainly. Usually a child who has a cyanotic spell would probably be expected to recover from that spell, not always, but the probability is high. This child never recovered, he continued to deteriorate and that again I think in my opinion speaks against the fact that this was simply a cyanotic spell, especially in view of the toxicological findings later.

Q But if those toxicological findings can be explained by the administration of digoxin after the cyanotic event, although one could expect him to recover, he could have died because of the injection of an overdose of digoxin after that





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event, could he not?

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A. Yes, but it would have to be

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very shortly after the event, or during that

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particular event, in my opinion.

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Q. Now, Doctor, I believe one of

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your concerns in the Justin Cook case are the levels

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that were found in the myocardial tissue, and indeed

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the levels in the tissue were quite high, they were

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in excess of 1100 nanograms per gram in one of the

samples?

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A. That is correct.

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Q. Now, you have recently published

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an article called: "Accidental Digoxin Overdose in

14

an Infant Post Mortem Tissue Concentrations", and I

15

believe this has been filed as Exhibit 276 in these

16

proceedings, do you have a copy of that article in

front of you, Doctor?

17

A. Yes, I think so.

18

Q. And it is a rather interesting

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article because it is not often is it that one is

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able to find an accidental overdose of digoxin when

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one knows the time of administration of the overdose,

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and is presented with such a wide range of toxicological

data.

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Now, I understand that in this case

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there had been a medication error, and that the child was administered a rather massive amount of digoxin instead of furosemide, was that the triggering event?

A. That is correct.

Q. And that from the time of administration until the time of death about 45 minutes elapsed?

A. Yes, that is the information that I was given.

Q. Now, were you given any information as to the time that this child suffered a cardiac arrest?

A. No, I don't know the exact time.

Q. Do you know whether the child underwent any resuscitation efforts?

A. I am sure, you know, this is routine in every hospital, but I don't know for how long a period of time.

Q. So conceivably the child was inadvertently administered the digoxin, suffered a cardiac arrest, attempts were made to resuscitate and then the child died and all those events would have taken 45 minutes, is that correct?

A. That appears to be the situation. The information that we got, the clinical information



















E.4

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2 was rather scanty really, this had occurred at  
3 another institution; and there was some question as  
4 to whether this 45 minutes indicated the actual time  
5 of death, or the time of the arrest, but to the best  
6 of my knowledge from what information I had I had  
7 assumed that this was the time of actual death,  
8 the child was pronounced dead, and I believe that  
9 the resuscitation period was rather short, maybe  
10 10 minutes or so.

11 Q After the administration of  
12 the drug, and after the death, I understand an  
13 autopsy was done and it was from that autopsy that  
14 you were able to analyze the tissue samples and come  
15 up with the data that you presented on page 484 and  
16 485 of the article; and the most striking data that  
17 are contained in that article are the data from the  
18 right ventricle and the left ventricle, where we  
19 see tissue concentrations of 1006 nanograms per gram  
20 for right ventricle; and 1252 nanograms per gram for  
21 the left ventricle.

22 Now, we know that the child was  
23 previously on digoxin intoxication; I'm sorry, was  
24 previously on digoxin therapy, for some three weeks  
25 or so. Notwithstanding that the levels that are  
found in the myocardial tissue are extraordinarily







E.5

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high, are they not?

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A. That is correct.

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Q. And would you agree with me  
that a fair portion of those levels probably would  
have been caused by the overdose of digoxin?

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A. Yes.

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Q. And so taking that one step  
further, a fair proportion of the levels in the  
myocardial tissue would have been caused by an  
overdose of digoxin some 45 minutes before death?

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A. That is what it appears, what  
the situation appears to be. I should perhaps point  
out that in our experience the therapeutic admini-  
stration of digoxin should not produce levels higher  
than about 450, so that everything in excess of 450,  
above 450 is very likely explained on the basis of  
this additional digoxin that was given.

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Q. And you say the therapeutic  
dose would not result in levels normally higher than  
450, is there any general range in which you expect  
to see tissue levels in the heart for a child who  
is on digoxin therapy?

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THE COMMISSIONER: Are these figures  
that we have here, are they not the general levels,  
the ones that you have in Table 1?





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THE WITNESS: Yes, I have some controls there. Babies who were receiving therapy, therapeutic dosages of digoxin and for comparison, and they are listed in Table 1 also.

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THE COMMISSIONER: That indication of plus or minus does that mean 180, I am taking the right ventricle for full-term neonates, 180 is the maximum and 84 is the minimum?

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THE WITNESS: No.

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THE COMMISSIONER: What does that mean?

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THE WITNESS: 180 would be the mean, and the number that follows it, 84, would be standard deviation.

14

THE COMMISSIONER: Oh, I see.

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MR. BROWN: Q. So for example, if we were to take the number for the left ventricle in your control group, on full-term neonates, you have a value there of 196 nanograms per gram.

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A. Yes, that would be the mean, the average level.

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Q. With a standard deviation of plus or minus 36?

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A. Yes.

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Q. So if one was to take 2 standard deviations, the uppermost extreme would be somewhere





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around 250, 260, would that be correct?

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A. Yes. In this particular group of only four infants that would be the case, yes, about 270 or so.

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Q. And would it be a fair interpretation of that then that although one might see in a therapeutic case digoxin levels in heart tissue of up to 450, on the basis of your control group it suggests that on the average the levels would be lower than 450?

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A. No, I cannot say that, because these were only 4 controls. You know, if I had taken another 4 babies the levels might have been higher, but they would not exceed 450, it would be extremely unlikely.

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There is one paper that I think I referred to earlier where levels higher than these were reported in babies receiving therapeutic dosages, a paper by Gorodischer, I don't know if it has been introduced as an exhibit here or not, Gorodischer is G-o-r-o-d-i-s-c-h-e-r, the spelling. He for some reason that I don't quite understand had considerably higher levels. I think Mr. Cimbura in his evidence indicated there was one level as high as 961, something in that order of magnitude. I believe a couple of





1  
2 others that had levels of 500 or 600, it was a small  
3 series, I think they were only 8 babies, but that  
4 was strange, it was out of proportion to everybody  
5 else's work. I feel quite confident that 450 is  
6 more or less the cutoff point for therapeutic  
7 administration.

8 Q So coming back then, Doctor, to  
9 this paper; on the basis of what you have said as  
10 to the range that you would expect in heart tissue of  
11 an infant on therapy, the administration of the dose  
12 of digoxin in this particular case resulted in a very,  
13 very substantial increase in the levels in the  
14 myocardial tissue over a period of about 45 minutes,  
15 and the difficulty we have with this case is we don't  
16 know exactly how much the increase was, it could have  
17 been 800 nanograms per gram, it could have been 1000  
nanograms per gram, is that not right?

18 A Yes.

19 Q And in dealing with the high  
20 levels in the myocardial tissue, I believe when you  
21 testified here the first day, and Mr. Lamek was  
22 examining you at that point and he was examining you  
23 on the concept of the time for distribution, the  
24 half time of distribution of digoxin into tissues. I  
25 will read to you an exchange that took place between







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Mr. Lamek and yourself. Mr. Commissioner, this can be found in Volume 75 at page 6597, and I guess this is as good a place to start as any:

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"Q. Is not the significance of the fixed heart tissue - I am sorry, the fresh heart tissue concentration this, that it precludes even the very small likelihood that the 72 nanogram level represented a level immediately post-administration?

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"A. In Justin Cook's case certainly, I think this is a very important confirmation of the existence of a massive overdose.

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"Q. Because it requires a period of time to have elapsed between dosage and death to have permitted distribution to the extent that was recorded in the fresh heart tissue, does it not?

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"A. That's right. The half time of uptake of the digoxin by the myocardium from the blood is approximately half an hour when the drug is given intravenously. So that if we had a level of 1000, let's say, and if this



















E.10

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2 "is - if the drug was given half an  
3 hour earlier, that means his ultimate  
4 level would have been 2000, but you  
5 are reaching half the expected  
6 myocardium concentration at that  
7 particular time. It does help you  
8 predict the time to some degree."

9 So I take it from that that it is your  
10 estimate that the half time, or the half life of  
11 distribution of digoxin from the serum into the  
12 myocardium tissue is 30 minutes?

13 A. I think there is a difference  
14 between the disappearance from the blood and the uptake  
15 into the myocardium. They are somewhat independent  
16 and the uptake in various tissues varies, varies  
17 considerably. So one cannot directly relate the  
18 disappearance of the alpha phase from blood with the  
19 uptake in tissues.

20 I read Dr. Kauffman's evidence, and I  
21 understand at some point he misquoted, or he has  
22 quoted me as saying that --

23 THE COMMISSIONER: It wasn't - it came  
24 from the --

25 MR. BROWN: Q. It came from the very  
article that we are dealing with.





E.11

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A. This very paper, that's right.

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Q. And I would just like to pursue this, if I could turn to page 483 of that article.

5

A. Right.

6

7

Q. In the section entitled "Discussions", the second full paragraph of that section.

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9

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MR. HUNT: Does the doctor have Dr. Kauffman's comments in front of him, if he is going to be asked about it.

11

12

MR. BROWN: I wasn't intending to put Dr. Kauffman's comments to the doctor.

13

14

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MR. HUNT: The matter has been raised by the Commissioner and now it would seem reasonable that the doctor have a copy of that, I think we can probably provide him with one.

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MS. McINTYRE: It is Volume 74.

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MR. HUNT: Volume 74, the page?

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MS. McINTYRE: Page 6415.

MR. HUNT: Pages 6412 to 6417.

THE COMMISSIONER: All right.





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MR. BROWN: Q. Mr. Hunt is going to provide you with a copy of Dr. Kauffman's testimony, doctor. If you wish to refer to it, you can. I hadn't intended to put the matter to you, but for your convenience he is providing you with a copy.

A. Thank you very much. I appreciate it.

Q. You could perhaps just put that to one side, doctor, and look again at the article. I directed your attention to the second full paragraph in the discussion section and the paragraph reads:

"Following intravenous administration the half time of digoxin distribution in various tissues, including myocardium, is 30 minutes."

If I might stop there, there is then a footnote, No. 10, and the Footnote No. 10 is a reference to an article by Doherty et al called "Clinical Pharmacokinetics of Digoxin Glycosides". You then proceeded:

"As a result one would expect 50% of maximal concentration to be present in the tissue in 30 minutes; 75% at 60 minutes; 87.5% at 90 minutes and





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94% at 120 minutes."

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Now that paragraph, doctor, I want to  
be clear exactly what you are saying there.

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Am I to take from that paragraph the  
proposition that 30 minutes after the intravenous  
administration of digoxin one would expect to find 50%  
of the maximal concentration of digoxin to be present  
in various tissues?

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A. That is correct, yes.

10

Q. And those various --

11

A. That is in myocardium.

12

Q. Yes.

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14

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A. That is in myocardium. I think  
it is not written very clearly or very well. But this  
30 minutes applies to myocardium and other tissues which  
have a similar time, uptake time.

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As you very well know the distribution  
of digoxin in the body, various tissues have different  
concentrations, and this is to some degree related to  
the uptake time.

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Some tissues will take it up very  
quickly, and in fact when you speak about central  
compartment or steady state situations, this is what  
you are referring to. The tissues that pick it up  
very quickly, such as liver, kidney, blood, are  
included in the concept of central compartment, whereas







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the myocardium is an example of a slow uptake situation, skeletal muscle also, where the uptake time or half time is about 30 minutes.

Q. Okay.

Well it is this proposition of 30 minutes that I would like to pursue.

The wording that you use here:

"As a result one would expect 50% of the maximal concentration..."

am I to take that to mean that that is a proposition that has been empirically proved or is this a hypothesis?

A. No, it has been proved.

We have done studies ourselves, not in humans. It is very difficult to do this in humans because it can only be done with radioactive digoxin, if you measure the uptake, and that is very difficult to do in humans. But in animals, in dogs, for instance, it is not difficult to do.

Actually I should not say the only way to do it is radioactive; we have done it with the routine way of taking biopsies of the myocardium.

What we did was we injected digoxin into the dog and then took biopsies of the myocardium at different times so we could measure the amounts.





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2 And the rate, the time of uptake, the half time, is  
3 approximately this, about 30 minutes.

4 This study that we did, we did not  
5 publish. I didn't like the data too much because there  
6 was a lot of variability and we wanted to repeat the  
7 study using radioactive digoxin, but it is an approxi-  
8 mate timeframe of about 30 minutes.

9 Q. In that particular study you  
10 did on the dogs, what was the rate of variability?

11 A. It was considerable. I don't  
12 have it here with me, but it was quite significant.

13 Q. So the --

14 A. When you measure tissue levels  
15 in any case your error in the measurement is higher  
16 than, for instance, when you measure blood. For  
17 several reasons: one, because you are dealing with  
18 higher levels and usually the error is more or less  
19 proportional to the magnitude of your measurement.  
20 Plus the fact that -- there are several factors that  
21 enter into consideration here.

22 When you take a biopsy or analyze  
23 a piece of tissue, the tissue has to be treated very  
24 specially or else if you squeeze it too much or dry  
25 it or the temperature is not appropriate, you get  
changes, physical changes in the tissue which may





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interfere.

Another factor which is important in this type of experiment is that it is not very easy to do because of the status of the dog. The dog may deteriorate during the experiment and that could change things, the acidosis and various chemical changes in the body. Therefore we didn't feel that it was, you know, all of very high quality, the data, and we haven't published it.

Q. And so on the basis of your empirical work then there appears to be a range of fluctuations, some difficulties with the data because of the fluctuation and also the fact that the empirical work was done on dogs and not humans, so to that extent would you agree that that work that you conducted would be inconclusive as to establishing the actual half time of distribution of digoxin into the myocardial tissues?

A. No, I wouldn't say it is conclusive. I would say that it is not a study that I would rely on completely, but I will -- I think it has to be repeated with radioactivity digoxin which is easier to measure.

Q. In fairness then, it is a starting point for further work but it is not conclusive





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of the proposition, is it?

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A. I think it is conclusive within a finite range of accepted variability, but I think any method you use you will find variability.

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If you take, for instance, the digoxin concentration in myocardium, you will find a fair amount of variation as you very well know. You just look at this data here.

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Q. Well, precisely, and if there is that variability as much as a difference of, let's say, instead of being 30 minutes, 45 minutes for the half time --

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A. It could very well be. It could also be 15 minutes in some cases. This is what variability is.

15

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Q. And to put it bluntly in view of variability we just don't know, do we?

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A. I wouldn't say we don't know. We have a range to work in that we have an idea of.

19

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In a specific individual it is difficult to be certain as to, you know, what portion of that range we are working in. It could be the lower end or the upper end or the middle.

22

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Q. Precisely. And if we are working in the upper end and let's say 45 minutes is







1  
2 the half time of the distribution of digoxin, if one,  
3 for example, in the case of Justin Cook saw that  
4 high myocardial level and the half life was 45  
5 minutes, one could reasonably say it would take longer  
6 perhaps than you expected for that level to be  
7 achieved in his heart tissue, could it not?

8 A. That is true.

9 Q. Conversely, if the actual half  
10 time is lower and about 15 minutes, it would take a  
11 much shorter period of time to reach that  
12 concentration, would it not?

13 A. It would take a shorter period  
14 of time but it would still take some time.

15 Q. I grant you that. It would  
16 certainly still take some time.

17 A. And the other factor is that  
18 we are relating these levels, the myocardial levels,  
19 to a maximum, and we don't know what the maximum  
20 would have been.

21 For instance, it could have been in  
22 Justin Cook's case, it could have been just 1,000; it  
23 could have been 2,000; it could have been 4,000, so  
24 if it were let's say 2,000, then this would be 50% of  
25 the final.

If it were 4,000 it would be only





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25% and so forth, you know, so we don't really know.

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Q. What it would be, and therefore any estimate as to the actual precise time of administration of that dose would be subject to the uncertainties that you just mentioned, would they not?

A. It would be subject to, yes, some uncertainties.

Q. And if I could just before leaving this article refer to the article that you quoted, which is Footnote No. 10, an article by Doherty.

A. Doherty, yes.

Q. "Clinical Pharmacokinetics of Digitalis Glycosides" appeared in "Progress In Cardiovascular Diseases".

I take it or is it your recollection that this was not an empirical study on actual tissue samples?

A. This article is just a review article. Dr. Doherty had done many studies. In fact he was the person who started doing studies with radioactive digoxin and he is considered the expert in work with radioactive digoxin.

This article is simply a sort of a summary of some of the work that he has done and work





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of others.

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Q. Is that the article you are

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referring to?

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A. Yes.

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MR. BROWN: Mr. Commissioner, could we have that marked as the next exhibit?

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THE COMMISSIONER: What number are

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we at?

9

THE REGISTRAR: 282.

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THE COMMISSIONER: Exhibit 282.

11

--- EXHIBIT NO. 282: Article entitled "Clinical Pharmacokinetics of Digitalis Glycosides".

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MR. BROWN: Q. If I could direct

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you to the second page of the article, Dr. Hastreiter, page 142, I take it that it is in this area that the estimates of the half life for distribution of digoxin in tissue appears; is that correct?

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A. Yes.

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Q. And in particular if I could

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refer you to the second column of that page, there is a sub-heading, "Intravenous", and if we go down to the bottom of that full paragraph, it says:

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"The dominant half time by this

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route of administration was determined

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to be 33 hours, not significantly

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different from that observed by the  
oral route.

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The exponential function (described previously) relating to distribution and tissue binding of digoxin, when applied to the intravenous serum curve, yields a half time of 30 minutes (line C), being bound nearly twice as fast as by the oral route."

11

You see where that appears?

12

A. I'm sorry, I don't think I am with you. Where is this?

13

14

Q. I'm sorry, we are on page 142.

15

A. Yes.

16

Q. And we are on the second column on the page.

17

A. Yes.

18

Q. And if you go down right to the bottom of that column to the first full paragraph --

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A. Yes.

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Q. -- the paragraph starts, "The exponential function".

21

22

A. Yes. Oh, okay. Could you read this again then?

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Q. Yes, certainly. It starts:

3

"The exponential function (described previously) relating to distribution and tissue binding of digoxin, when applied to the intravenous serum curve, yields a half time of 30 minutes (line C), being bound nearly twice as fast as by the oral route."

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Now am I correct then in interpreting

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that paragraph as suggesting that the half time or

11

the suggested half time of distribution of digoxin to

12

the tissue is approximately 30 minutes?

13

A. That is right.

14

Q. That estimate, however, you would agree is based on an exponential function?

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A. Most of these uptake rates are exponential functions.

17

Q. And just to be precise as to

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what an exponential function is if I could refer you

19

again back to page 142 of the article, the first

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column this time, please, and if you would go about

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three-quarters of the way down to the sentence starting, "Also shown is the exponential function...". Do

22

you see that sentence?

23

A. Where is this? I'm sorry.

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Q. Page 142. It is in the first  
full column.

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A. Yes.

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Q. And it is about two-thirds of  
the way, the "T $\frac{1}{2}$ " appears.

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Q. Then the question starts.

A. Oh, yes.

Q. "Also shown...".

A. Yes.

Q. That area reads:

"Also shown is the exponential function representing the half-time of the distribution and binding of the drug..."

And I think he is referring to the diagram that appears on the bottom of the page, "...obtained...", and that is the exponential function:

"...obtained by subtracting the values shown from the extrapolated serum curve (line B)..."

referring to the graph.

"...from the descending limb of the actual serum concentration (curve A)..."

again referring to the graph.

"...thus eliminating metabolism and excretion and leaving behind only that portion of the curve relating to distribution and binding of this drug to tissue (line C). Since this is really where the therapeutic





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effect takes place, one is unable to estimate the onset of therapeutic activity through knowledge of this function. By the oral route of administration, the half-time of distribution and binding is 50 minutes, so we estimate that at this time about 50 per cent of digoxin is bound to tissue and, at 2 hours, about 75 per cent has arrived at the sites of action."

Now, would you agree with me that in calculating the exponential function relating to the half time of distribution of digoxin to the tissues, what has been done in this study is simply a mathematical exercise, that one has taken the extrapolated serum curve which they label line B, subtracted that from the values on another curve A and have come up with a third curve C, and on the basis of that third curve C they postulate that the half time of distribution of digoxin into the tissues is, in the intravenous case, 30 minutes. Is that a correct interpretation of the exercise that they performed?

A. Yes, that is correct. That is the way it used to be done before we used computers to







1  
2 analyze these curves. Nowadays usually what we do is  
3 simply take the serum data and have the computer fit  
4 it to what we call a bi-exponential, sometimes three  
5 exponential curve and thus these things can be pre-  
6 dicted more accurately and easier and more rapidly.

7 Q. But nonetheless it is a pre-  
8 diction based upon a mathematical exercise, is it not?

9 A. It is.

10 Q. And in this particular case it  
11 does not appear to be supported by empirical data,  
12 does it; empirical data as to the concentrations in  
13 tissue, as to the actual time it takes digoxin to get  
14 into the tissues? This is really just an extrapolation  
15 based on the disappearance of digoxin from the serum,  
16 isn't it?

17 A. Yes. As far as the concentration  
18 and uptake of digoxin in tissues, I would agree with  
19 you. I don't think the quotation that was given in  
20 the paper is very good because this paper is making a  
21 sort of indirect assumption.

22 I would agree that this is based on  
23 blood studies and not direct tissue studies. Dr.  
24 Doherty said himself, as I said, who is the expert in  
25 the radioactive digoxin, he started doing them and he  
performed several studies on tissue concentrations and









1  
2 we probably should have quoted another of his studies  
3 where he deals with this more specifically.

4 Q. There is another area that I  
5 wanted to canvass with you again. It was the work that  
6 you had said that you had just conducted regarding the  
7 volume of distribution in a certain group of children,  
8 infants, I'm not sure. I believe you said that you  
9 had conducted some studies to determine the volume of  
10 distribution in children at various points of time  
11 and that you had data for 1 hour and 3 hours but the  
12 study was not yet published.

13 A. No, I didn't say that. This  
14 is a paper that we have here.

15 Q. I'm sorry, I don't have it.

16 A. It is an exhibit and it is  
17 called "Digoxin Pharmacokinetics in Premature Infants".  
18 From the data that is furnished in this specific  
19 paper one can more or less calculate for this parti-  
20 cular group of babies the various volumes of distribu-  
21 tion at specific time intervals. The time intervals  
22 that are given here, as I indicated yesterday, are 1,  
23 3, 12, 24 and 48 hours.

24 THE COMMISSIONER: I'm sorry, this is  
25 an exhibit?

MR. BROWN: It is Exhibit 268,





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apparently, Mr. Commissioner.

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THE COMMISSIONER: 268.

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MR. BROWN: Q. So, it was on the basis of the data that you obtained published in this paper --

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A. That's right.

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Q. -- that you were able to suggest that 1 hour after times zero, the volume of distribution would increase by approximately 2?

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A. Yes.

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Q. And that after 3 hours it would increase by fivefold?

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A. That is 5 times the so-called volume of central compartment.

14

Q. Yes, yes, I appreciate that.

15

A. Yes.

16

17

Q. But am I clear, Doctor, in taking it that the calculations you made there for the increase in the volume of distribution were based on the data that you obtained for premature infants in this paper?

18

19

20

A. I think there were six; six.

21

Q. Six premature infants?

22

A. Yes.

23

Q. So, the study group upon which

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1  
2 you are basing those suggested increases in the volume  
3 of distribution are a study group comprised of pre-  
4 mature infants?

5 A. That's right. However, there  
6 have been many other studies done on volume of  
7 distribution in older children, newborn babies that  
8 were mature as well as older infants and the volumes  
9 of distribution are definitely higher than those of  
premature babies.

10 Q. Well, I think you have shown  
11 that quite graphically in this paper, that is, the  
12 difference in the volume of distribution between the  
13 different age categories.

14 A. That's right.

15 Q. But have those same studies  
16 done on the other children, the neonates and the  
17 children, do they perform the same exercise that you  
18 have, that is, 1 hour after times zero one can  
19 expect the volume of distribution to increase by 2;  
after 3 hours by 5?

20 A. I don't know of any specific  
21 babies where this was done. You can take, if you know  
22 the dose that was given and if you have values at  
23 these specific times, blood concentrations, you can  
24 do that, you just have to have a series of babies of  
25





1  
2 different ages, weight groups and so forth and do the  
3 same exercise. I don't have any direct information  
4 here with me but I can assure you that, you know,  
5 having an idea of what the volume of the central  
6 compartment is in older, more mature babies versus  
7 premature babies, one could very simply I believe  
8 perform these calculations for the other groups also.

9 Perhaps I should indicate that I  
10 believe it was in Dr. Kauffman's evidence also that  
11 this data for volume of central compartment here of  
12 0.6 average, 0.62, was used as one of the values  
13 published in the literature and it so happened that  
14 this data is much lower than most of the others  
15 because the others have values as high as usually  
16 around 1.3. But what was not mentioned I believe,  
17 at least in the portion that I read, was that these  
18 are small premature babies.

19 Q. Yes.

20 A. And it is different, they have  
21 smaller volumes of distribution. The more mature  
22 babies have volumes of distribution which are around  
23 1 and the little older infants would have it  
24 probably in the order of 1.3; that is volume of  
25 central compartment I'm talking about.

Q. Well, is it possible then,





1  
2 Doctor, that the rate of increase in the volume of  
3 distribution over time may differ between premature  
4 infants and full-term neonates?

5 A. Yes. It is in fact very likely  
6 that they will differ a little because premature  
7 babies have a longer half life for the drug, they  
8 don't excrete the drug as readily as the older  
9 children. So, yes, there is a difference, but the  
10 difference is predictable, I don't think it would be  
very...

11 Q. Well, all I'm suggesting,  
12 Doctor, is that when trying to calculate the dose of  
13 digoxin administered to a child and where one of the  
14 assumptions is that the volume of distribution will  
15 increase at a certain rate over time, the data that  
16 you were using were based on the data in your paper  
17 that is taken from premature infants, and it is quite  
18 possible that the data for neonates would give us  
a somewhat different reading?

19 A. This is the only data I have  
20 available here with me.

21 Q. All right.

22 A. Therefore, I cannot use anything  
23 else. I think there have been studies on volume of  
24 central compartment for older babies or more mature  
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babies. So, that much we know.

As far as the time relationship, yes, it is likely that in more mature babies the change will be a little more rapid; not a lot. That depends of course on the degree of prematurity of these babies and it depends on the age of the other babies we are talking about because it is related to the half life of elimination of the drug.

Q. Well, perhaps we can stop there at this point, Doctor, and continue after the break, Mr. Commissioner.

THE COMMISSIONER: Yes.

MR. BROWN: I do not intend to be that much longer, fifteen to twenty minutes.

THE COMMISSIONER: Yes. All right. Well, we will take twenty minutes.

--- recess.







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--- Upon resuming:

THE COMMISSIONER: Yes, Mr. Brown.

MR. BROWN: Thank you, Mr. Commissioner.

Q Dr. Hastreiter, if you could turn please to the case of Allana Miller. Again in the case of Allana Miller you were asked to perform a similar exercise as to estimate the time, the route and the dose of digoxin administered to this child.

Now, Volume 76 of your evidence, at page 6649, we covered this ground, and this was during Mr. Lamek's examination in chief of you, and I will read to you part of your testimony where this was covered; starting on page 6649, line 7, you were asked the question:

"Q. Yes. And you said, and this is at page 73 also, that if the dose were administered by IV bolus injection, page 73, I am sorry, you said that if the intravenous medication was used, the expected onset of the effects would have been from 5 to 30 minutes, that is so, and it was your opinion that you would think the dose to have been given about half an hour before the time of this child's arrest; the arrest





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"having occurred at 2:45?

"A. I think that would be a good, reasonable assumption.

"Q. Dr. Hastreiter, how do you know that, or, how can you form that opinion?

"A. If one assumes that the cardiac arrest resulted from digoxin intoxication, and if the dose was given intravenously; and knowing what the time expectancy would be for the effects to occur following an intravenous bolus, the initial effect would be observable by 5 to 30 minutes, and the peak effect from 30 minutes to 4 hours, or from 1 to 4 hours essentially. You would have to work within that time frame more or less. Usually what we do is use sort of average values and medium values to try to get as close as possible, knowing full well that the error can be very large.

"Q. Isn't the difficulty with that that you have to start by assuming the very thing that is in issue, that is to





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"say that the arrest was caused by digoxin intoxication?

"A. In my opinion this is a valid assumption in the child that is not expected to have an arrest and who develops one and then has a very high blood digoxin level.

"Q. I guess the difficulty I am having is this, and you must help me with it if you can, please; is that in the absence of evidence of distribution of the dose to tissue, one cannot preclude the possibility that dose was administered very shortly before death?

"A. True.

"Q. And not prior to the arrest?

"A. Oh, I see. Yes, there was a considerable interval between the arrest and the death.

"Q. The arrest was at 2:45.

"A. And death?

"Q. And death was around 3:27 ... "

Now, Doctor, in reading that, am I accurate in saying that in the case of Allana Miller





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it would be your best estimate that the digoxin would have been administered by an intravenous route, and it would have been administered about half an hour before the time of the child's arrest at 2:45?

A. From five minutes to half an hour before the arrest at 2:45.

Q. Quite so, within that time limit, but the benchmark that you are using in fixing the time would be, am I correct, the arrest which occurred at 2:45?

A. That is correct.

Q. Could I ask you please to turn to the medical record of Allana Miller, and I believe the Registrar has placed a copy of that on the table before you. If you would please turn to page 42 of that record, and these are progress notes kept on the child, and if I can refer you please to the note dated:

"March 20/81 1900-0300."

If you would go to half way down the note to the sentence starting: "At approximately", it reads:

"At approximately 0145 babe's apex was noted to be 54 and very irregular (BP was 98/p). Child was stimulated and apex came up to 70's. This







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"happened 3-4 times. Then the child began to gag and vomit large amounts of very thick clear mucus. She was suctioned for further amounts of this mucus."

There is an asterisk:

"Respirations became quite laboured.

Sub ... ",

I am sorry "Sub", I can't read that: " ... and inter-costal ... ", and again I can't read that:

"... very noticeable. Dr. Soulioti came to examine the child and administered Lasix 6 milligrams IV push at 2:40."

Now, the only question I have of you, Doctor, is that given those recitations of the events that Allana Miller underwent, would it not be possible that the symptoms that Allana Miller began to demonstrate at approximately 0145 in the morning could well have been the manifestation of digoxin intoxication?

A. I think this is a possibility.

Q. It is a possibility. Indeed if those symptoms were taken to be the benchmark, or the time of the onset of the symptoms of digoxin





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intoxication, would it then be possible to calculate back from that point of time, that is 0145, the estimated time of administration of the digoxin?

A. Yes. It would be the same way if it had been given intravenously you would assume that it was given 5 to 30 minutes prior to the onset of the symptoms.

Now, the one finding I think that militates against this hypothesis would be the fact that the blood level was so high, and I think it is difficult to conceive that the child would have remained alive having a blood level of this magnitude, for a long period of time, because it was 78 nanograms per millilitre in post mortem blood.

Q. Yes, somewhere around 68 to 70, so that would be your concern in this case?

A. Yes, that would be a very important consideration I believe.

Q. Well, if I might then read to you the opinion of Dr. Kauffman?

A. Yes.

Q. On this child.

This, Mr. Commissioner, is found in Volume 71, and I will be starting to read on page 5690.

THE COMMISSIONER: Was that during Miss Cronk's examination?





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MR. BROWN: Yes, it was during her  
direct examination.

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MR. YOUNG: Would the doctor like to  
have a copy?

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THE WITNESS: If you have an extra one  
it would be good.

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THE COMMISSIONER: Yes.

THE WITNESS: Thank you very much.

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MR. BROWN: Q. Would you turn please  
to page 5690, Doctor?

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A. Yes.

Q. And I will be beginning to read  
at line 16:

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"Q. Doctor, this may be something that  
you can help us with and it may not,  
but again, we have two time intervals  
here that are at least recorded in the  
progress notes. At 1:45 we see the  
irregularity in the child's apex and  
the gagging and the vomiting to which  
you have referred but it is almost an  
hour later - well, it is indeed an hour  
later when it is noted that she began  
seizure-like activity. When you talk,  
Doctor, of the onset of the critical





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"symptoms, do you have one of those  
two specific times in mind?

"A. Well, I was actually relating  
the onset to the increase in bradycardia  
and irregular heart rate and the  
gagging and vomiting. I think that  
could have been the onset of the  
symptoms that had progressed to the  
other symptoms that followed. There  
is a complicating factor and, that is,  
because of her rapidly deteriorating  
condition, the seizures could possibly  
be related not to digoxin but to lack  
of oxygen or acidosis or other things  
that were intervening over that short  
period of an hour when she was rapidly  
deteriorating.

"Q. Doctor, is it then your best  
judgment, bearing in mind that the  
gagging, the vomiting and the brady-  
cardia that you have mentioned are  
recorded as having occurred or at least  
starting to occur at 1:45 in the  
morning, is it then your best judgment  
that this dose would likely have been







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"administered about an hour before that time?

"A. I can't be precise about the hour but I would agree that it was most likely administered prior to the onset of those symptoms which appear to be the beginning of a series of worsening symptoms. It could have been as early as 30 minutes, maybe probably within an hour.

"Q. All right.

"A. I said in my report I gave outside numbers of 60 to 90 minutes to be generous but I really believe it was probably shorter than 90 minutes."

Now, having read that passage, Doctor, it would appear that Dr. Kauffman took as his benchmark for the onset of symptoms of digoxin intoxication those events which apparently began around 1:45 in the morning.

Now in light of what Dr. Kauffman has just said, do you agree or disagree with the opinion that he has put forward?

A. I cannot disagree with this opinion, because as we have - as I and others have





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2 indicated earlier the symptoms of digitalis toxicity  
3 are not specific enough to allow us to really be  
4 certain as to the exact time of the onset.

5 Q So really then is it fair to  
6 say that we are left with a possibility that those  
7 events at 1:45 could well have been the onset of  
8 digoxin intoxication, and administration occurred  
9 prior to then; or we have another possibility that  
10 they were the manifestation of her clinical stage  
11 and that the digoxin was administered at some later  
12 time, are those the two possibilities that we are  
13 left with?

14 A Yes.

15 Q If I can now turn to the case  
16 of Kevin Pacsai, please, Dr. Hastreiter. Yesterday,  
17 you were again questioned about this child by Mr. Lamek,  
18 and I don't know if you have a copy of your --

19 A I think I have got one.

20 Q ... of your testimony from  
21 yesterday?

22 A No, I don't.

23 Q The parts I will be directing  
24 your attention to are found in Volume 76, Dr. Hastreiter.

25 THE COMMISSIONER: That is the day  
before yesterday.





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MR. BROWN: I am sorry, my notes are out of date, Mr. Commissioner, it was two days ago.

THE COMMISSIONER: Yes, all right.

MR. BROWN: Q. Volume 76, commencing at page 6692.

MR. YOUNG: Excuse me, Mr. Brown, I gave him the volume for yesterday.

MR. BROWN: Oh, I am sorry.

THE COMMISSIONER: 6692 is Volume 76, do you have that one?

THE WITNESS: I don't have it.

MR. YOUNG: I believe that is the volume Mr. Brown was reading from just a moment ago.

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Far be it from me to suggest anything that might add to the expense of this exercise, Mr. Commissioner, but maybe having regard especially to the fact that the Atlanta people are coming I suppose some time in the foreseeable future and this exercise will probably be repeated, it probably wouldn't be a bad idea to have an extra copy of the evidence for the witness.

THE COMMISSIONER: I think it is an excellent idea, but the expense is a problem. You see these charming ladies coming out in mink coats with all the money we are giving them! We will see what we can do about that.

How many does the Commission get now, do you know? I am not talking about all the ones that are distributed.

MR. LAMEK: We have four. You have a set - yes, I think we have four.

THE COMMISSIONER: Well, surely one of those could be made available.

MR. LAMEK: One of those, of course, as Dr. Bryson points out is with Mr. Kelly doing his summary.

THE COMMISSIONER: Yes, so we have three, and I have taken one of them.

MR. LAMEK: You wouldn't want to use







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mine for the witness with all the markings on it.

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THE COMMISSIONER: No. Well, the idea is certainly being taken into consideration.

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MR. BROWN: Q Dr. Hastreiter, if I might direct your attention to page 6691, starting at approximately line 15, Mr. Lamek began to examine you as to the time, dose, route exercise on Kevin Pacsai, and he asked you:

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"Do you have an opinion as to the most likely route and method of administration to this child?

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"A. I think this is difficult to say in this particular baby, more so than any others we have covered so far because the level was not extremely high. It was considerably lower than in the others, and this time relationship here between this event at 4 o'clock, 4 a.m., and the time of the baby's death was six hours spread which is a long time compared to the others, so it is conceivable that various methods of administration must be considered I think. One would be an intravenous bolus; the other one would be possibly





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"even oral administration although that would be probably difficult because the baby had no nasogastric tube of any tubes in the GI tract which would facilitate the administration of medication.

"I wouldn't rule out the possibility of a continuous infusion even because of the level not being so terribly high.

"Q. Are you able to express a view as to the most likely of those routes? I certainly don't ask you to if you don't feel comfortable.

"A. No, I would say from a practical standpoint probably the easiest way to administer the drug would have been intravenously, bolus intravenously because the child had IV's in place and it would just have been a matter of injecting the drug into the system - through the system. Also faster and less detectable perhaps than the other routes.

"Doctor, if that be the most likely





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"route of administration it would follow from what you told us yesterday that the first effects of toxicity would likely have been manifested anywhere from 5 minutes to half an hour after the dose?

"A. Right.

"Q. If you are therefore correct that at 4 o'clock the first detected signs of toxicity appeared that would place administration somewhere between 3:30 and 5 minutes to 4?

"A. Right.

"Q. In that range of time?

"A. Yes.

"Q. Obviously these are not watertight compartments.

"A. Yes."

Now in reviewing that testimony, Doctor, is it fair to say that the reason you selected the intravenous bolus as the most likely route of administration was simply its practicality?

A. That is correct.

Q. Well, in view of the length of time between the manifestation of something at about





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4 o'clock, the arrest at close to 9 o'clock and the death at 10 o'clock, would it not, Doctor, perhaps from a pharmacological point of view be more reasonable to assume that this was not an intravenous bolus injection but an oral administration.

A. I think one could make this assumption. It is not my favourite one but it cannot be ruled out.

Q. I take it the reason it is not your favourite assumption is - or that the oral is not your favourite assumption is simply the practicality?

A. Yes, it would be somewhat difficult to administer the medication to a child that has no nasogastric tube in place. You would not be able to push the medication through the tube. You would have to give it orally, either placing it in the bottle or squirting it in the baby's mouth or something of that category which I think would be rather impractical.

Q. Well, when Dr. Kauffman testified here, Dr. Hastreiter, he again was asked to go through the same exercise that you went through, and during his examination by Miss Cronk which appears in Volume No. 72, starting at page 5786.







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MR. YOUNG: Again, I will hand the volume to the witness.

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MR. BROWN: Q I am sorry, if we could again turn back one page to 5785, Doctor, starting right at the bottom of that page at line 22.

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A. Yes.

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Q Dr. Kauffman was asked this question:

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"May we deal first, Doctor, with your conclusions regarding the likely method of administration of the drug?

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"A. I couldn't be certain on this child whether it might have been given by injection or orally. I think the possibility is equal either way. I felt from his course as described in the chart that it was unlikely that he received a large bolus close to the time of his death and that impression was affirmed by the fresh lung tissue specimen, which indicated to me that there had indeed been significant distribution to the tissues prior to his death.

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"So I really couldn't make a





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"distinction between whether or not he might have received a dose parenterally or orally.

"Q. Are the digoxin concentrations found both in the fixed and frozen tissues of this child, Doctor, consistent in your view with a dose administered several hours prior to the onset of his critical symptoms?

"A. I think it is consistent with several hours prior to or even a little bit longer.

"Q. Well, you have told us, Doctor, that it was your opinion having regard to what you perceived to be the distribution of digoxin to tissues that a large bolus administered intravenously was unlikely. Were you able to put a time frame based on the information available to you on the most likely time of administration of the drug?

"A. I really couldn't pin it down very well. When I looked at it, I had the impression from looking at the





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"description of the events over approximately a 12-hour period prior to his arrest that there was something happening as early as 3:30, 3:45 that morning when the nurse described him as being very different from what he had been before and being limp and so forth. It appeared to me that that could possibly be the beginning of intoxication symptoms which then progressed over the subsequent hours to varying degrees of dysrhythmia, ultimately culminating in an arrest from which he could not be resuscitated.

"If I accepted that relatively slow progression of events rather than the sudden catastrophic description which existed in some of the other cases, then it made more sense to me that he might have received a dose orally some 6 to 12 hours prior to the onset of this dramatic change in his condition. But I couldn't pin it down with any confidence more tightly than that.

"Q. Doctor, what are you regarding as





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"the onset of this change in his clinical condition that you have described?

"A. In that scenario I was regarding the change in his condition described at approximately 3:45 to 4 o'clock the morning of the 12th of March."

Which was approximately the same bench mark that you used, Doctor.

The question that I want to put to you is that do you agree or disagree with Dr. Kauffman's suggestion that it made more sense to him that the child might have received a dose orally from 6 to 12 hours prior to the onset of this dramatic change in his condition?

A. I believe that he indicated that it made more sense to him.

I think this is a very difficult decision to make, and really we don't have enough evidence to support one or the other hypothesis extremely well.

I still feel that the practicality of giving the oral preparation would be a factor to consider here and this was a main reason that I opted against it.







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Q Well --

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A But it is not by any means an  
indication that I would throw it out or rule it out.

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Q Well, strictly from the clinical  
and pharmacological point of view, would Dr. Kauffman's  
opinion also be equally possible?

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A Yes, it would be.

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Q Just one last area that I would  
like to explore with you, Doctor. It has to do with  
Baby Gary Murphy.

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Yesterday during your examination by  
Mr. Lamek he raised the question of Gary Murphy with  
you, and I don't know whether you have your testimony  
in front of you but it is contained in Volume 77. Do  
you have Volume 77 there?

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A I have it. Thank you.

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Q There were a couple of comments  
that you made during the course of your testimony I  
would like to pursue if I could direct you, please,  
to page 6931. Around line 7 Mr. Lamek started  
questioning you:

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"Q All right. But apart from that  
perhaps greater propensity to develop  
pre-renal failure in the case of Gary  
Murphy, the two distinctions that you





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"have suggested, Doctor, don't explain  
the levels in Gary Murphy, do they?

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"A. Oh, certainly.

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"Q Well, the fact that one has a  
normal heart --

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A. Excuse me, what are the two distinctions we are talking about?

Q. I believe the two distinctions were a structurally normal heart, in the case of Baby Pacsai, as contrasted to the horrible type of congenital anomaly found in Baby Murphy. I believe the second one, and this would be found at page 6930, Dr. Hastreiter, I believe the second one was that Baby Pacsai had pre-mortem levels, the fact that he had pre-mortem levels was the second distinguishing factor. But I believe on examination by Mr. Lamek you agreed that if we took Gary Murphy we probably would be able to calculate pre-mortem levels in the 10 to 15 range, which might well be the range for Kevin Pacsai.

Those I believe were the two distinctions.

Line 12:

"Q. Well, the fact that one has a normal heart and better able to resist toxicity."

"A. No, no, that doesn't explain the level."

"Q. No, it doesn't explain the level."





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"A. No, that doesn't explain the level, but the pre-renal failure -- no, the normal heart explains the good renal profusion."

"Q. Yes, okay."

"A. And therefore the lack of propensity to develop pre-renal failure. On the other hand, I think it is quite conceivable that in Gary Murphy a level of, let's say, between 10 and 15 pre-mortem would have been explained on the basis of pre-renal failure. It is not a common event, although high levels are common in pre-renal failure. This level of magnitude may be a little excessive. I have never seen elevated post mortem levels. I have seen pre-mortem levels around 10 or perhaps higher, I am sure I have seen them higher than 10 pre mortem associated with renal failure.

So, that to me would be the best explanation. I should, however, emphasize that I think we are talking







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about different periods of time and different circumstances. I think when we look at the other children, as I have said earlier, my main concern was not to miss any cases that possibly could have been intoxicated. Here I think we had a situation a year later or so where the Hospital was monitoring the children very, very closely. The Hospital was aware of the problem and so forth and we were also concerned about, you know, not calling a case toxic when the possibility of non-toxicity existed."

Now, you recall those comments,

Doctor?

A. Yes.

Q. And I think then if you could please turn to page 6943 of your testimony. Having described the circumstances under which you were looking at the Gary Murphy baby and your efforts to not call a case toxic when non-toxicity existed as a possibility, again, Mr. Lamek examined you on 6943, beginning at line 7:





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"Q. When we speak of Murphy and Pacsai, or Murphy and Estrella, or any of those people, I am obliged to follow up something you said a moment ago, Dr. Hastreiter, because I think it goes to the way in which we must approach all of the expert evidence we have heard.

You referred to a couple of points of distinction between Gary Murphy and Kevin Pacsai. Is it also an important point of distinction between the two that when Kevin Pacsai died, and especially when his chart was reviewed, the atmosphere was one of great suspicion. Your task you very forthrightly said was to look for any possible suggestion of digoxin intoxication in those charts. We were looking for an explanation and an apparent epidemic and there had been murder charges already laid.

When Gary Murphy died, when his case was reviewed and the inquest was held, although there was obviously





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enormous concern and apprehension,  
the climate if I may say so appeared  
to be to dispel suspicion if it were  
possible to do it, to explain matters  
that might otherwise be suggestive  
of an overdose.

Believe me, Doctor, I don't  
want to be offensive, I am not sug-  
gesting any conscious lack of  
objectivity on your part or on any-  
one else's part, but can we be sure  
that the climate may not have  
influenced judgment in marginal  
cases?"

"A. No, I don't think we can. I  
think we had great pressures placed  
upon us in Gary Murphy's situation,  
where there was a great deal of, as  
you say, apprehension, not only local  
but also public apprehension and it  
was a very difficult decision to  
make."

Now, the only question I have,  
doctor, what were the pressures that were placed upon  
you?





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A. Well, the only pressures that were placed upon me was the public apprehension about the situation of the babies being intoxicated at the Hospital receiving overdoses. At that particular time this was in focus, there was every day something appearing in the papers, in the news and so forth. I think it was an important facet.

If we had said that this baby had been intoxicated, the reaction that would be expected would be I think from the public or the press and so forth would be considerable. All I am saying is that we had to be very cautious as to every detail, the wording, defining everything very clearly. I think another difference was that in Gary Murphy's case I believe the workup had been completed, there was no other toxicological evidence forthcoming, or nothing else that we could do really to better pinpoint the situation, whereas, in the other babies' cases we were looking still for evidence.

So, there was this difference which I think is important. Here we have a complete case and we have to make a decision on the basis of what we have. In the other, we had still a way to go, or the possibility thereof anyway.

Q. So, at least in your own mind







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2 when you were reviewing the Muprhy case and you were  
3 testifying you apprehended that the consequences of  
4 finding toxicity in this child would be grave and  
5 that that indeed may have played some factor in your  
6 decision?

7 A. I don't think it played a  
8 factor in my decision, but it made our decision, our  
9 whole handling of this particular case to be  
10 exceedingly cautious to a degree that every word and  
11 every manoeuvre made was, you know, had to be clearly  
12 explained and justified and so forth.

13 Q. When you gave your best  
14 opinion at the inquest of Gary Murphy, it was that  
15 the elevated digoxin could probably be accounted for  
16 by pre-renal failure, and I believe yesterday during  
17 the course of Mr. Lamek's examination we reached the  
18 conclusion that while that might be a hypothesis the  
19 biochemical data to support that hypothesis was not  
20 present, that the only biological data that you really  
21 had were from three weeks prior to the date of his  
22 death; is that correct?

23 A. There was not laboratory  
24 confirmation or the presence of renal or pre-renal  
25 failure at the time of the baby's death. We had an  
earlier episode which occurred, I don't know if it was the





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6th of March or April I think, the baby died on the  
23rd I believe, two weeks earlier.

Q. Nonetheless, that remained as  
your hypothesis as to the cause of death, or as to  
the elevation of the digoxin levels in that child?

A. Please?

Q. I said, nonetheless, that re-  
mained as your hypothesis of the cause of the elevated  
digoxin levels in that child?

A. That is correct.

THE COMMISSIONER: Does the absence  
of biochemistry indicate there was no pre-renal  
failure or does it tell us nothing?

THE WITNESS: I believe that the  
last examination we had was on the 21st, the laboratory  
data.

THE COMMISSIONER: Yes.

THE WITNESS: On the 21st, and the  
baby died on the 23rd. So, I think the laboratory  
data indicated there was no evidence of pre-renal  
failure.

THE COMMISSIONER: Well, whatever you  
want to say, when the laboratory tests, do they  
establish in your mind that there was no pre-renal  
failure on the 21st, is that correct, is that what you





J9 2 are telling me?

3 THE WITNESS: At least they don't  
4 confirm the presence of pre-renal failure.

5 THE COMMISSIONER: Well, that is  
6 really what I want. Are they conclusive or not?  
7 Can you have renal failure without the laboratory  
8 tests showing it up?

9 THE WITNESS: Yes. You can have  
10 transient pre-renal failure, low cardiac output without  
11 having changes. The BUN, or urea nitrogen, would be  
12 the one finding that I would be looking for, parti-  
13 cularly, and that can be normal during the early  
14 phases of pre-renal failure, or during a transient  
15 episode of pre-renal failure.

16 MR. BROWN: Q. So, indeed, what  
17 occurred may have been transient and wasn't disclosed  
18 in the biochemical reports, is that what you are  
19 suggesting?

20 A. That is my hypothesis, yes.

21 Q. So, it is possible that what  
22 caused the elevation of the digoxin levels in Gary  
23 Murphy was some process that did not manifest itself  
24 in the biochemical data, but nonetheless was present  
25 in the child, is that fair?

A. You see, in the absence of  
more concrete findings, this is my best hypothesis at





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2 this point. I can't find good evidence to support it  
3 but concerning all the clinical hypotheses which are  
4 as poorly supported as this one, or worse, I would  
5 stick with this one as the best one. I would consider  
6 this one to be the most acceptable from a clinical  
7 standpoint and possible explanation for the blood  
8 level, the biochemical or, let's say, the digoxin  
findings in this child.

9 Q. And then Mr. Lamek put Dr.  
10 Kauffman's hypothesis to you about this slow process  
11 of decay and I believe yesterday you expressed some  
12 disagreement with that and stated that it was a good  
13 theoretical speculation but you thought that in practice  
14 it would be very difficult for him to prove that.

15 So, really, Doctor, at the end of  
16 the day --

17 MR. YOUNG: Well, let's have the  
page reference for that.

18 MR. BROWN: Q. Page 6942, Doctor.  
19 Start at page 6941 at line 10:

20 "Q. Yes. Now, do you have a view  
21 on the likelihood of that..."

Referring to Dr. Kauffman's proposition.

22 "...being a, well, do you regard it  
23 as an acceptable explanation of the  
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elevated digoxin levels?"

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"A. Well, as you know, I have great respect for Dr. Kauffman. I really like him. I think he is a very good pharmacologist. I don't quite agree with him here because I think it is very hard to prove what he is saying and this is my disagreement.

It is a good theoretical speculation, but I think in practice it would be very difficult for him to prove that. My hypothesis of renal failure has not been proven by any means either, but at least it is a practical everyday situation that we encounter. I am not sure at all that what Dr. Kauffman said occurred. It occurs in theory but whether it occurs to the point where you would see elevated levels of this magnitude, nobody knows."

Are you really saying then, Doctor, that you disagree with Dr. Kauffman's hypothesis and that the hypothesis that you are putting forward you think is the most practical but it hasn't been proven?





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A. That is basically correct.

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I cannot completely prove it. I preface it by saying that I do have great admiration for Dr. Kauffman but here I disagree with him because I just think that my hypothesis is a more practical one, one that occurs in clinical practice more often and his is a very good one if it could be proven but it hasn't been proven.

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Q. And you thought that your hypothesis was practical and possible and would it be fair to say that in the view of the climate of the time when you were trying to, that you had great concern about the finding of toxicity, and we are looking for possible explanations for non-toxicity, that that swayed your mind and that your opinion then at the inquest was that there was a possible explanation, natural explanation for the elevated digoxin levels in Gary Murphy?

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A. Maybe you had better repeat your question, please.

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Q. I'm sorry. You have said that Dr. Kauffman's hypothesis you felt was theoretical and would be difficult to prove in practice?

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A. Yes.

Q. And you said that your hypothesis





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although not proven is practical. Am I correct in saying that on the basis of your feeling at that time you were therefore of the opinion that that provided a possible explanation for the elevated digoxin levels in Gary Murphy?

A. That is correct.

Q. And was the conclusion you reached in that case also in part influenced by your frame of mind at that time when you were looking for possible explanations of non-toxicity for the digoxin levels in this child?

A. I think perhaps at an emotional level. I cannot really say that anyone has complete control of the emotions. I try to not let it interfere in my decision but, you know, whether I consciously did or not, I cannot be one hundred per cent sure.

Q. Would it be fair to say that where there was perhaps an element of doubt in your mind and that you envisaged a possible explanation under the circumstances of the time you went with that explanation?





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A. I think the circumstance of doubt should be - the circumstances of the possibility of doubt exists in practically any situation, there is no total certainty in any of the cases we have ever dealt with, I don't believe.

Q. And so on the concrete case of Gary Murphy where there was an element of doubt you went with non-toxicity rather than toxicity?

A. Because I felt that this was a better explanation.

MR. BROWN: Thank you, Doctor.

THE COMMISSIONER: Thank you, Mr. Brown. Miss Forster.

CROSS-EXAMINATION BY MS. FORSTER:

Q. Doctor, I am Elizabeth Forster and I act for Phyllis Trayner. I take it, Doctor, what you have told us earlier, that you were first approached regarding the deaths at the Hospital for Sick Children in May, 1981 by Dr. Tepperman?

A. Yes.

Q. And you have told us that you were asked to examine the medical records of some of the babies from both a medical and a toxicological point of view to determine what cases raised a







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suspicion of digoxin intoxication, and in what cases you could rule out any suspicion, is that correct?

A. Yes, that is so.

Q. Can you tell me how these instructions were communicated to you?

A. Well, I was invited to come to Toronto and meet with members of the Police Force, and the Crown, and the Coroner's Office and I did this.

We met, and I was told about the situation, what had occurred earlier, and that it was very important to go through the charts. I examined the charts carefully, to try to determine which babies could be completely excluded and which babies should not be completely excluded from further investigation because of the probability of a digoxin overdose.

Q. Were your instructions ever put down in writing?

A. I don't believe so, no.

Q. Now, in preparing these first reports, the one you did in May, 1981 and the subsequent amendment, I take it you had before you the medical records of the children; any laboratory data that was available; and you also





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2 received the information from Mr. Cimbura as it  
3 became available, is that correct?

4 A. As it became available, yes.

5 Q. Did you have any other  
6 information given to you, or any other information  
7 available from which you prepared these first reports?

8 A. Well, I had been told a  
9 little bit about the non-medical circumstances of  
10 this situation, but I didn't use any of this  
11 information to make medical decisions.

12 Q. Who told you, who gave you  
13 this non-medical information regarding the circum-  
14 stances?

15 A. The members of the Police  
16 Force, the Crown and the Coroner's officer.

17 Q. And was any of that information  
18 in writing?

19 A. No. None of it was in writing,  
20 I was shown some, for instance, lists of babies  
21 that were being investigated by them. I was shown  
22 some references regarding the nurse that had cared  
23 for that particular baby and things of this sort;  
24 which room the baby had been in; what time the  
25 terminal event occurred; and at what time the  
death occurred and at what time the baby died; some





1  
2 general facts of this type.

3 Q. And you mentioned you were  
4 shown some references about nurses, are those the  
5 nurses that were caring for the children?

6 A. Yes.

7 Q. Was that told to you, or were  
8 you given some written material?

9 A. No, there was I believe a  
10 chart available with this information.

11 Q. Were you given that chart?

12 A. No, I just looked at it.

13 Q. Did you make notes based on  
14 the information you gleaned at the meetings with  
15 the Police and the Crown and what you saw from this  
16 chart?

17 A. No.

18 Q. Doctor, I notice in your  
19 report, for example, at page 21.

20 A. Which volume is this?

21 Q. Pardon me?

22 A. Which volume?

23 Q. No, your report, Doctor, the  
24 bound copy of your reports?

25 A. Yes.

Q. On page 21.





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A. Yes.

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Q. Dealing with the paragraph dealing with Jennifer Thomas, the last sentence you have on Jennifer Thomas says:

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"Miss Nelles was on the ward but not directly caring for this infant."

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Doctor, I have looked through the chart of Jennifer Thomas and I can't find any reference in the chart to the fact that Miss Nelles was on the ward but not caring for the infant, and I am wondering where you got that particular piece of information?

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A. I really don't remember. If it was not in the chart I must have got it from one of the, either the police officers, or the coroner, or maybe the Crown Attorneys perhaps during a discussion of the case.

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Q. Was this particular report prepared after the meetings?

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A. Yes.

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Q. Did you go back to your office and dictate this report?

A. Yes.

Q. And if you didn't take notes of the meetings that you had with the Police and







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2 the Crown, can I take it that this kind of thing,  
3 such as the references to somebody being on the  
4 ward but not caring for the child, is something  
5 you put in your report from memory?

6 A. No. I may be wrong, maybe  
7 I did take some notes later, after I had extracted  
8 this information from the chart. It is possible  
9 that subsequently we may have gone over this  
10 information and that I may then have taken some  
11 notes, that is probably what happened.  
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Q And do you know if you still have those notes, or could you say if you might have them?

A No, I don't have the notes. We typed these summaries and then I didn't think the notes would be much use.

Q Now after this report in 1981 and the revision you made to it, you indicated to us that you conducted another review of some additional babies in the summer of 1982. How were your instructions regarding that report communicated to you?

A It was after the preliminary hearing, right?

Q Yes.

A There was a meeting, a meeting of again members of the Police Force, the Crown Attorneys and I believe also members of the Coroner's staff, and the investigation at that time was significantly expanded to incorporate many more babies, and I was asked again to review the medical situation, the medical records, laboratory data and toxicological data if available.

Q And were any of your instructions with respect to this report put down in writing?





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A. No, I don't believe so.

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Q At the meetings that you had with the Police, or the Coroners, or the members of the Crown Attorney's Office, were you given any additional information except for the fact that there be additional babies included in this report?

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Q Again, was any of this information in writing, or was it verbal?

A. No.

Q And did you take notes at this meeting or series of meetings with respect to the second report?

A. No.

Q And I take it that this report was based on the same information you had for your first report, the medical records; the laboratory tests; and the material from the Centre of Forensic Sciences?

A. Yes.

Q And you told us that in completing





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the second review, and in particular in completing the first page of the form in which you rated each child, you tried as best you could to complete this from a clinical point of view and disregard the toxicology, is that correct?

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A. That is true.

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Q. And would you agree with me, Doctor, that in some respects you were at a disadvantage in going through this exercise in that you were never able to see the child when he was alive and observe his clinical condition?

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A. Yes, definitely.

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Q. And would you also agree with me that the treating physicians or nurses, or any medical personnel that had contact with the child may have noticed subtle changes in the child that would not be reflected in the medical records?

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A. That of course depends on the quality of the medical records and a number of other factors with the person who was watching the baby.

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THE COMMISSIONER: The doctor too, I guess.

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THE WITNESS: The physician?

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THE COMMISSIONER: I shouldn't ask you, but we find in our profession sometimes some are better than others.

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THE WITNESS: Yes, sure.

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MS. FORSTER: Q. You indicated it depends on the quality of the medical records?

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A. And the personnel caring for the infant.

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Q. And some medical records may be more detailed than others?

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A. Yes.

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Q. And some --

A. Some parts of medical records are more detailed than others, and the entire record -- sometimes one record may be superior to the other.

Q. And some entries in the medical records may be prone to misinterpretation?

A. I am sure that can happen, very rarely, I don't think it should happen.

Q. But it can simply from reading another person's note of what happened?

A. Yes.

Q. There is room for misinterpretation.

A. I think everything that is done by humans there is room for errors in interpretation.

Q. And I take it, sir, that in classifying a child, or putting him in the category of "good" on your form, the main criteria you used

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were the suddenness of the death and the unexpectedness of the death put together, so it was really one criteria, is that right?

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A. It is not that simply. I think it had to do with the type of lesion that the child had. It had to do with the other intercurrent illnesses are not present. The clinical course of the infant up until the time of his terminal event happened, and so forth. This was important, these two facts that you mentioned were very important in characterizing the terminal episode, but there were many other factors.

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Q. And simply in characterizing the terminal episode, if the treating physician were to tell you that he didn't regard the death as unexpected, would that cause you to at least reconsider your opinion with respect to a child in some cases?

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A. I would have to find out a lot more about the reasons for it.

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Q. Well, I understand that Mr. Scott is going to be putting a great deal of the treating physician's evidence to you and I will leave it to him to do that. Can we turn, Doctor, to the case of Allana Miller?

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THE COMMISSIONER: It is -- whenever you like. It is not quite one o'clock and if Allana Miller is going to take any more than, say, five minutes, it might be wise to rise now.

MS. FORSTER: I think it may take a few more.

THE COMMISSIONER: Yes. All right. How long do you think you will be, Miss Forster?

MS. FORSTER: I would think fifteen to twenty minutes, sir.

THE COMMISSIONER: Yes.

Miss McIntyre, how long will you be?

MS. MCINTYRE: I will only have a very few questions.

THE COMMISSIONER: Miss Jackman?

MS. JACKMAN: I can't see that I would be any more than half an hour.

THE COMMISSIONER: I think probably that will solve our problem because we are going to rise at roughly twenty to four this afternoon. So I think that means your great motion, Mr. Labow, I will be able to avoid making a decision on it.

MR. LABOW: I think that is wonderful.

THE COMMISSIONER: All right then. Until 2:30. --- luncheon adjournment.





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--- on resuming at 2:30 p.m.

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THE COMMISSIONER: Yes, Miss Forster.

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MS. FORSTER: Q. Dr. Hastreiter,

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I was about to turn to the case of Allana Miller,

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and you may recall that the medical record for

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Allana Miller indicated that in the morning she died  
she was to receive 6 mg. of Lasix at 2:40 a.m. and then  
suffered seizure activity at 2:45.

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Mr. Lamek asked you about the

possibility of confusion between digoxin and Lasix,  
and as I understand your evidence you indicated that  
if a volume, a similar volume of digoxin had been  
confused with the same volume of Lasix you thought  
that the concentration of digoxin that would have been  
administered to the child would have been too small  
to result in the levels that were seen in this child.

Have I correctly summarized your --

A. I wonder if we should look at  
this.

Q. Sure. Did you want to look  
at your evidence or the medical record?

A. Yes. The evidence.

Q. Perhaps I will ask you what  
your evidence is because I don't have the page  
reference.







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3 As I understand it yesterday Mr.  
4 Lamek asked you about the possibility of confusion  
5 between the Lasix and the digoxin and you gave an  
6 answer based on a confusion of a similar volume of  
7 Lasix and a similar volume of digoxin.

8 Could you repeat what your evidence  
9 was in that respect?

10 A. I don't remember.

11 Q. Okay. Well, do you think it  
12 likely that the --

13 MR. OLAH: Is that the Miller child?  
14 I might be able to assist.

15 MS. FORSTER: Yes.

16 MR. OLAH: It is found at page 6665,  
17 Volume 76.

18 MS. FORSTER: Thank you.

19 Q. At page 6665, doctor.

20 A. Yes.

21 Q. Mr. Lamek asked you:

22 "I don't ask you to speculate on the  
23 likelihood that that happened here,  
24 but if it did occur and if indeed at  
25 2:40 in the morning what was thought  
to be 6 mg. of Lasix in fact was  
translated into an equivalent volume





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2 of parenteral digoxin and I will ask  
3 you to calculate the dose that that  
4 would involve, could that in your  
5 opinion have caused the arrest of  
6 Allana Miller five mintues later?"

7 And you answered:

8 "A. I don't believe so because the  
9 Lasix, the concentration of a vial  
10 is 1 to 10 mg. per ml., I believe.

11 Yes. And..."

12 A. It should be 10 mg. per ml.

13 Q. Okay.

14 "...And 0.6 ml. then..."

15 And the Commissioner says:

16 "I'm sorry, doctor, the concentration  
17 was what did you say?"

18 And you answered:

19 "10 mg. per millilitre. So -- or  
20 6 mg. of Lasix would be 0.6 milli-  
21 litres, and 0.6 millilitres of let's  
22 say the adult solution of digoxin  
23 which contains 0.25 per ml. would be  
24 1.5 mg., approximately what we  
25 calculated earlier for Justin Cook  
also."





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A. This should be 0.15 mg., not  
1.5.

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Q. 0.15?

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A. Yes.

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Q. All right.

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THE COMMISSIONER: Which contains --  
it is not per millilitre. 0.15 --

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THE WITNESS: Which contains 0.25 mg.  
per ml., it should be.

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THE COMMISSIONER: milligrams, 1.5 --

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THE WITNESS: 0.25 mg. per ml.

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THE COMMISSIONER: Would be 1.5 mg.  
is that right?

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MR. FORSTER: Q. Is it .25 per ml.  
would be .15 mg.?

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A. It would be .15 mg.

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Q. All right.

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A. Because we are talking about  
less than a ml.

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Q. All right.

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A. We are talking about 0.6 ml.

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Q. Okay. And then you continue:

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"A. Would be 0. -- what did I say?"

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"Q. Let's go through the calcula-  
tion."

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"A. 0.15 mg., 150 micrograms. I think for Cook I have said in the neighbourhood of 200. It is more exactly 6 times 0.025, which would be 0.15 mg."

"Q. Yes."

"A. Or 150 micrograms."

"Q. Yes."

"A. This is too small a dosage in my opinion to result in the blood levels we are talking about some time later which would have been a good hour later or so."

So I take it from that answer, doctor, that in your opinion it is unlikely that there was a confusion of similar volumes of Lasix and digoxin; is that correct?

A. That is correct.

Q. During your exchange with Mr. Lamek you also referred to your article which has been marked Exhibit 276 on the accidental digoxin overdose in an infant. Do you have that in front of you?

A. Yes.

Q. And this is a case as I understand it where a child was given 2 mg. of digoxin







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instead of 2 mg. of Lasix; is that correct?

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A. Yes.

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Q. And you were careful to point out that this child was not in your hospital. Was it hospitalized in a hospital in the United States?

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A. Yes.

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Q. And the concentrations of digoxin are somewhat different in the United States, and I wonder if you could tell me first of all how many vials would it take to give a dose of 2 mg. of intravenous furosemide?

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A. Well, the concentration of the adult vial I believe is the same, 0.5 mg. in 2 ml., so it would take four of those vials to reach 2 mg.

15

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17

Q. Of furosemide?

A. Oh, I'm sorry.

Q. I am asking about the furosemide first.

18

19

A. I am thinking about --

Q. Digoxin?

20

21

A. No. It would take 4 vials of the adult digoxin preparation to correspond to 2 mg. of digoxin, but if you --

22

Q. Right.

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A. -- if you wish to compare volumes?

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Q. No. First of all the question I wanted to know from you, doctor, was in a dose of 2 mg. of intravenous furosemide --

A. Yes.

Q. -- how many ampoules are we talking about?

A. 2 mg.?

Q. Yes.

A. Less than an ampoule.

Q. Less than an ampoule?

A. 1/5 of an ampoule because it is 10 mg. per ml. and there is 1 ml. in one ampoule I believe.

Q. All right. And you said in order to obtain a dose of 2 mg. of digoxin you would need to administer four adult vials. And how many pediatric vials would that be in the United States?

A. It would be -- in the United States the concentration of the pediatric vials is 100 instead of 50 micgrams. Therefore it would be 20.

Q. 20?

A. Yes.

Q. And do you happen to know whether this child was given adult or pediatric digoxin?

A. No, I don't.





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Q. In this case, however, there was a confusion between concentrations of different drugs as opposed to volumes; is that right?

A. I don't know the circumstances really involving the error in the dosage.

Q. All right.

Well, would you agree with me, however, that instead of this child getting 1/5 ampoule of Lasix it received at least 4 and perhaps as many as 20 depending on whether we are talking of adult or pediatric ampoules of digoxin?

A. Yes.

Q. And that was done accidentally?

A. That is what I was told, yes.

Q. And I take it from what you said you can't help us as to the circumstances under which this accident occurred?

A. No.

Q. Now in the Miller case if a similar accident occurred such that rather than being given 6 mg. of Lasix the child, as the child in your report was given 6 mg. of digoxin, we would be falling within the range that you have stated in page 25 of your report.

At page 25 of your report you estimate





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the possible amount of digoxin that could have been  
administered to this child.

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A. Yes.

5

Q. And your range is 2.5 to 7.5  
mg. Is that correct?

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A. I don't see it on page --

8

Q. I'm sorry, I'm talking about  
your report, doctor.

9

A. You mean this one?

10

Q. Yes. On page 25.

11

A. Okay.

12

THE COMMISSIONER: That is assuming  
a steady state is the note I have.

13

MS. FORSTER: That is right.

14

THE COMMISSIONER: Yes.

15

16

MS. FORSTER: Q. And you speculate  
that the range of amounts of digoxin that Allana  
Miller could possibly have received to be between  
2.5 and 7.5.

18

19

A. Yes, but as I explained  
yesterday this would be assuming steady state.

20

Q. That is right.

21

22

A. And also assuming a volume of  
distribution of 16 litres per kilogram which is as  
high as one could go. I think perhaps more realistically

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2 one could take 10 instead of 16, and that would bring  
3 the figures down by 1/3. So the range would be  
4 perhaps 1.8 to 5, but -- yes, this is what I said at  
5 the time.

6 Q. If, however, the Miller child  
7 had received a dose of 6 mg. of digoxin at 2:40 in-  
8 stead of 6 mg. of Lasix, could that account for the  
9 levels you saw in this child?

10 A. If she had received 6 mg. of  
11 digoxin?

12 Q. Yes.

13 A. Oh, that would be a very large  
14 dose, yes, certainly.

15 Q. Thank you.

16 Could we turn next to the case of  
17 Jordan Hines and page 48 of your report, doctor, under  
18 the heading "Cause of Death" --

19 A. Yes.

20 Q. -- you indicate "no satisfactory  
21 cause of baby's death was found. SIDS does not  
22 explain the arrhythmias."

23 In reaching the conclusion about SIDS,  
24 and I take it you rejected that because of the ar-  
25 rhythmias you saw in this child --

A. That's right.





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Q. -- did you have regard in making those comments to the autopsy report that is found in the child's chart? Do you have the child's chart in front of you?

A. Yes.

Q. The autopsy report, the preliminary autopsy report is found at page 28.

A. Yes.

Q. If you look at the third to last sentence on page 28, it says:

"This pathologic evidence in conjunction with the clinical history makes the diagnosis of a missed-SIDS a possibility. However, this does not explain the arrhythmias and further conclusions will have to await examination of the conduction system."

A. Right.

Q. Did you have regard to that portion of the autopsy report in preparing your conclusions, doctor?

A. No. I considered the pathologist's findings. I didn't consider the pathologist's opinion and I don't think -- I considered it to some degree I am sure but not -- usually pathologists are





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not clinicians and I like to make my own opinion.

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Q. The reason I ask you is your wording of "SIDS does not explain the arrhythmias" is very similar to the language used by the pathologist and I wondered if you were adopting his conclusions or it is a conclusion you came to on your own?

A. I believe that I came to this conclusion on my own. I don't think a pathologist really should draw clinical conclusions generally.

Q. Have you had much experience with SIDS victims, doctor?

A. Yes.

Q. Have you done any research into the --

THE COMMISSIONER: Excuse me a moment. Pathologists, are they not supposed to determine the cause of death?





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THE WITNESS: Yes. But usually the pathology reports contain a clinical pathological relation at the end because very often the pathologist alone ---

THE COMMISSIONER: Yes, they do and I think that these reports generally seem to have that too, they have clinical diagnoses and pathologic diagnoses?

THE WITNESS: Yes.

THE COMMISSIONER: But they are expected are they not to - well, not expected, it is not required, but they generally do give a ---

THE WITNESS: They get together with a clinician, or they should, usually, to at least get all the clinical information that they can from the chart, from the medical record, and then try and put that information together with the pathological findings and arrive at a conclusion. But I think my objection here would be for the pathologist to say that the findings, or the SIDS possibility does not explain the arrhythmias. I don't think this is their domain really to say, not without the support of a clinician.

MS. FORSTER: It is a conclusion with which you agree though, I take it, Doctor?







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A. Yes, I agree.

3

Q. Have you personally done any  
research in the area of SIDS?

4

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A. No.

6

Q. What is the extent of your  
involvement with the condition?

7

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A. Taking care of patients,  
patients with heart disease are sometimes mistaken for  
patients who have no heart disease and occasionally  
the patient will turn out to have SIDS, plus the  
fact that most paediatric cardiologists will rotate  
through a general paediatric service for some time  
during the year and take care of general paediatric  
patients also.

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Q. All right. And you indicate  
that you thought it was a diagnosis that is properly  
made by a clinician as opposed to a pathologist, is  
that correct?

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A. That is true, yes.

19

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Q. Are you aware of anything in  
the literature or from your own experience of any  
signs or pathological indicators of SIDS?

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A. Yes, there are some supportive  
evidence at pathology such as was described here:  
thickening of the pulmonary arterials, the musculature,





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2 increased extramedullary hematopoiesis, blood  
3 production, and brown fat. I think this was what  
4 was described here, this other sort of classical  
5 findings.

3  
6 It is my understanding that it takes  
7 time to develop. So, it is really one of either  
8 a missed-SIDS where it took about two weeks for  
9 these findings to develop following the episode or  
10 it was a completely undiagnosed situation perhaps  
11 earlier but where the child did develop findings  
12 and then died.

13 Q. Well, to the extent that there  
14 are these pathological indicators, do you not  
15 consider it an appropriate exercise for a pathologist  
16 to review them and come to a conclusion as to  
17 whether ---

18 A. I think they are supportive  
19 evidence. I don't think they are in themselves  
20 indicative of the problem unless you can exclude  
21 other causes of death, and that is the problem of  
22 SIDS, it is a diagnosis that is made by exclusion  
23 of everything else.

24 Q. Were you able to determine  
25 the cause of death for this child?

A. Excuse me, just a second,





1  
2 let me look at this. I don't think that anybody  
3 was able to really determine the cause of death.  
4 I think we are dealing with probabilities again  
5 here and this child had a structurally normal heart,  
6 had arrhythmias before his death and died  
7 unexpectedly at that time and we felt that the  
8 possibility of digoxin overdose was very high.

9 Q. All right. But as you said,  
10 we are dealing with the case of probabilities and  
11 one probability or possibility as a cause of death  
12 is digoxin intoxication. We don't know in this  
13 case how much the child received and whether it  
14 was a lethal dose, would you agree?

15 A. Yes. Well, when we speak  
16 about probability we have a scale. This is not to  
17 say that the child had the probability of this,  
18 that and that, I think the probability of digoxin  
19 toxicity here is very high.

20 Q. All right.

21 A. And that has to be taken  
22 into consideration. How much digoxin the child  
23 received we don't know, and we don't have blood  
24 values I believe in this baby to help us.

25 Q. All right. And is it not  
also possible though, Doctor, that the child could





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have died from SIDS or missed-SIDS?

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A. As I said before, SIDS is

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a diagnosis made by excluding other causes.

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Q. Yes.

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A. This is a child - okay, against

7

the diagnosis of SIDS are the following facts:

8

(1) That the child had a disease which was not

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completely worked up but which appears to be a

10

disease of the condition system of the heart, so-called Sick Sinus Syndrome.

11

Now, secondly, the child had a

12

structurally normal heart, died suddenly. Now,

13

this could simulate SIDS except that digoxin levels

14

were found in his tissues and the presence of

15

arrhythmias earlier and the fact that digoxin was

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found in the child's tissues is I think very

17

Q. All right. Well, let's

18

suppose for a moment that we had no information

19

at all on digoxin with respect to this child.

20

Would you agree that it is a possibility that the child died of SIDS or missed-SIDS?

21

A. I would not, you know,

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completely exclude it. It would not be my first

23

diagnosis. I think I would really like to know

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1  
2 more about the circumstances of this child's  
3 death, what exactly happened, because the child  
4 had, he was after all in the Hospital because of  
5 a problem which had to do with his conduction  
6 system and I would imagine that he was being  
7 monitored quite closely.

8 As I said, SIDS is a diagnosis of  
9 exclusion. If a child is found dead without a  
10 reason, or maybe even in the Hospital, if a child  
11 is being watched and dies suddenly, if there are  
12 certain risk factors in the family or in the  
13 siblings or if the child is premature, prematures  
14 have 10 times higher probability for being a  
15 candidate for SIDS, which this child was not, and  
16 things like this. I don't see, you know, if you  
17 put all these things together, these facts, that  
18 your probability for SIDS is very high just because  
19 the child dies suddenly.

20 Then you could take any child who  
21 dies suddenly, whether there is a cause or not,  
22 and if you look for a toxicological cause  
23 and don't find it, then you could call it SIDS,  
24 but it is not SIDS if you can demonstrate that  
25 the poison was given to the child.

Q. All right. I am sorry, I





1  
2 wanted to go back to one thing you said. Did you  
3 say one of the things that would affect your  
4 judgment is whether or not siblings had been at risk  
5 of SIDS?

6 A. Yes. If the child itself  
7 had previous missed-SIDS, so-called missed-SIDS  
8 episodes, if there are siblings in the family who  
9 died of SIDS and if the child was a premature  
10 infant, because prematures are pre-disposed, are  
11 more susceptible to sudden death than other children,  
12 there are other factors such as apnea, unexplained  
13 apnea episodes.

14 Q. It also places the child at  
15 higher risk of dying of SIDS?

16 A. Of SIDS, yes. Now, this baby  
17 is different because as far as we know had no apnea.  
18 He had bradycardia. Now, bradycardia frequently  
19 will follow apnea. If the child stops breathing for  
20 some time the heart rate will come down. This  
21 association of apnea and bradycardia is quite common  
22 in SIDS patients who eventually will die of SIDS,  
23 especially premature babies. But the bradycardia  
24 alone, without apnea such as occurred here, to me  
25 is an important finding. It is quite different  
from the situation that you usually find in SIDS.





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Q. When we are talking about  
bradycardia, are you talking about it during the  
terminal episode?

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A. No, I am talking about brady-  
cardic episodes that occur earlier.

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Q. In the absence of information  
on digoxin then what would be your opinion as to the  
cause of death of this child?

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A. Since this child had a  
specific disease which was not fully worked up and  
fully diagnosed, but the specific condition was a  
disease of the conduction system, probably Sick  
Sinus Syndrome, my interpretation would be that  
the child died as a consequence of this problem.  
The child either developed a slow rate and stand-  
still or developed a severe tachycardia because  
it can go either way, it can be very slow or very  
fast.

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Now, tachycardias are usually more  
easier to pick up and they would probably have been  
described in the record if it had taken place.

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So, my feeling would be then that  
the child stopped, the heart stopped as a consequence  
of the disease of the sinus node conduction system  
and by definition then you cannot use SIDS as a





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2 diagnosis because SIDS is an unknown etiology, you  
3 don't know, you don't have a reason, an obvious  
4 reason for the child's death.

5 Q. Well, Doctor, I would like to  
6 put to you the evidence of Dr. Becker who wrote  
7 the autopsy report on this child, and perhaps your  
8 counsel can provide you with a copy of Volume 38  
9 of Dr. Becker's evidence.

10 MS. CECCHETTO: I don't have a copy.  
11 Here you are, Doctor.

12 THE COMMISSIONER: Whose examination  
13 was that?

14 MS. FORSTER: It is the examination  
15 of Miss Cronk.

16 THE COMMISSIONER: Yes.

17 MS. FORSTER: Q. At page 7657 starting  
18 in the middle of the page, Doctor, Miss Cronk  
19 says:

20 "Q. All right. Doctor, we see on  
21 the preliminary autopsy report at the  
22 top of the page under the informational  
23 section as to date and time of death  
24 the words 'Query Sudden Infant Death  
25 Syndrome'. Can you help me, Doctor,  
what you meant at that stage by







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"inserting those words at the top of  
the preliminary autopsy report?

A. The query did not refer to the  
diagnosis of Sudden Infant Death  
Syndrome but was referring to the  
mode of death, the mechanism of death.

Q. All right. Can you help me  
as to what you mean by the mechanism  
of death in that context?

A. Well, the last four lines of  
the autopsy report are referring to  
an explanation for the way that the  
hypoxia, chronic hypoxia may have  
interfered with respiratory function  
and ..."

I am sorry, I don't have the volume.

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1  
2 I am sorry:

3 "...in other words, this was the  
4 hypothesis that we were suggesting."  
5 And then turning, doctor, to page

6 7667.

7 A. Page 7667, you say?

8 Q. Yes, but starting at 7666:

9 A. Yes.

10 "Q. And then you continue in the  
11 sentence that I began to read:

12 'This pathological evidence, in con-  
13 junction with the chemical history...'"

14 I think that should be 'clinical history':

15 "'...makes the diagnosis of a missed-  
16 SIDS a possibility.'

17 Doctor, you have told us what  
18 the pathological features were;  
19 indeed you have set them out ex-  
20 pressly in the report that you were  
21 referring to. What elements of the  
22 clinical history in the case of  
23 Jordan history of Jordan Hines were  
24 you referring to in that sentence?"

25 "A. My I go over that sentence?"

"Q. Yes."





Hastreiter  
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"A. This is the way I would put it together.

This pathologix evidence, referring to the chronic hypoxia, in conjunction with the clinical history, referring to the recurrent apnea, makes the diagnosis of a missed Sudden Infant Death Syndrome, implying the missed Sudden Infant Death Sundrome to mean in support of the apnea hypothesis as a possibility or hypothesis for the mechanism of death."

And then down later on the page, the last question, Miss Cronk says:

"Q. And when you refer, doctor, to a diagnosis of missed-SIDS as a possibility, did you then have doubt in your own mind as to whether or not the terminal diagnosis for this child should be missed-SIDS?"

"A. No. The diagnosis was clearly missed-SIDS, but I am talking here about the mechanism of death. How did the apnea actually produce it and





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how does the apnea or can the apnea explain the other two things that have been mentioned in the history, the bradycardia and the tachycardia, so I am trying to put this together into some anatomical or pathological basis."

"Q. What possibility, doctor, were you referring to when you made use of the word 'possibility' in that sentence?"

"A. Using that as a hypothesis that the apnea was a possibility, and what I meant was that my hypothesis in the situation was that the neural control in the brain was abnormal and this abnormal neural control of respiration could account for the apnea.

On the other hand the apnea alone or per se probably could not easily account for the bradycardia and the tachycardia. I knew that the bradycardia is closely associated with the apnea, but less often so with the tachycardia.







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And then a question:

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Therefore I was very interested in this case because it suggested to me that the neural control of cardiovascular and respiratory function was abnormal, and therefore accounted for the apnea, the bradycardia and the tachycardia, and under microscopic sections I had evidence that there was scarring in the very region of the brain that is associated with this neural and cardiovascular control.

Now, in order to confirm this hypothesis I wanted to show that the conduction system of the heart was normal."

"Q. Well, doctor, that is a very long answer and I am not sure that I have at all understood it fully.  
"THE COMMISSIONER: It is a medical answer to what was essentially a question in English.

The question was what did you mean by a possibility? Does that





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conceivably mean that there is some other possible explanation? I would think that is what it meant but I may be wrong."

"THE WITNESS: Sure. The other possibility would be that there could be something wrong with the conduction system."

"THE COMMISSIONER: Yes?"

"MS. CRONK: Q. I take it, doctor, that when you made that reference in the preliminary autopsy report you were of the view that at least one of the possible explanations was a problem in the conduction system of this child?"

"A. Very unlikely possibility, but in order to prove any other -- in order to prove the neural hypothesis I wanted on an academic basis to rule out the conduction defects of the heart."

"Q. And there was then in your view I take it some slight doubt that the terminal diagnosis at that stage





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should be described as missed-SIDS?"

"A. No, there wasn't any doubt in my mind about the diagnosis."

"Q. Right. You continue in the next sentence and I will return to that in a moment, doctor, to indicate: 'However, this does not explain the arrhythmias and further conclusions will have to await examination of the conduction system.'

Doctor, there has been suggested in evidence -- well, perhaps I should ask you first: What arrhythmias were you directing your mind to, doctor?

"A. I was using arrhythmia in the broader sense to include rate. I was referring to slow rate, bradycardia, or fast rate, tachycardia."

"Q. Were you aware, doctor, of the nature of the terminal events sustained by this child?"

"A. Approximately, but not in detail."

"Q. Were you aware that ventricular fibrillation had been recorded in the medical record as having been





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And then the next page:

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experienced at the time of death?"

"A. Yes. I assumed that was a  
terminal event."

And then down a bit further on page

"Q. Were you at that stage, doctor,  
having regard to the language which  
is in your report, uncomfortable about  
the finding there had been arryhtymias  
in the situation which you felt to  
be attributable to death by missed-  
SIDS?"

"A. No. I was quite happy with the  
bradycardia being present in relation  
to the apnea, but as I mentioned, the  
tachycardia I think is less common,  
and I was interested in trying to find  
an explanation for why the apnea,  
bradycardia and tachycardia all  
occurred together."

"Q. I take it, doctor, from the  
balance of your sentence that you  
felt that that puzzle to you might  
be explained by the conduct of an







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examination of the conduction system?"

"A. It may have helped to explain it, but it wouldn't have explained everything. But if I could have proved that it was entirely normal, then it would have --

"THE COMMISSIONER: Doctor, if you could have proved that it wasn't?"

"THE WITNESS: If I could have proved that the conduction system of the heart was normal then that would have meant that my hypothesis for the neural control of respiration being abnormal would have been more viable. But this was certainly in an academic sense."

THE COMMISSIONER: Yes. Is it a question, Miss Forster?

MS. FORSTER: Yes.

Q. Doctor, as I read Dr. Becker's evidence, he is raising the question of the arrhythmias as you did, but as he explained in an academic sense, to explain precisely the symptoms that you indicated had caused you some concern.

A. Yes. Perhaps I should emphasize that the apnea is an important finding here,





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2 and perhaps I did not refer to it as such earlier, at  
3 least not emphasize it as much as it should have been.  
4 But otherwise I would disagree in some respects with  
5 the report here. Because, first of all, the tachy-  
6 cardia is not explained. Dr. Becker mentioned that  
7 he could explain the bradycardia secondary to the  
8 apnea, but could not explain the tachycardia, so  
9 something is missing there; and the baby had severe  
10 tachycardia, there is no question about that.

11 Secondly, I think it is well known  
12 there are cases of sick sinus syndrome which is also  
13 called bradycardia/tachycardia syndrome, because you  
14 have the two extremes, where no pathologic findings  
15 are present, it is a functional situation. So the  
16 absence of pathologic findings is not that critical.

17 Thirdly, I think the findings in  
18 the central nervous system are interesting, but they  
19 are not that specific. I mean, they could explain  
20 the apnea but they may not explain the apnea. I  
21 don't think the correlation between these two has  
22 really been totally established.

23 So I think there is still something  
24 missing in this explanation here. And as I said  
25 earlier, I think if you ask -- I am by no means -- I  
don't consider myself an expert in SIDS, but if you





1  
2 ask different people you will probably here that  
3 many will feel that this is a diagnosis of exclusion,  
4 you have to exclude other situations.

5 Q. Doctor, is it your evidence  
6 that only once you have excluded all other explana-  
7 tions can one rely on a diagnosis of SIDS?

8 A. No. You know, everything is  
9 possible and it is not impossible that a child may  
10 have a disease, and then in addition on top of it  
11 develop SIDS, I am not saying that this is not  
12 possible, but it would be already a very rare co-  
13 incidence. Since we here have already a situation  
14 where it is potentially, could be potentially fatal,  
15 the sick sinus syndrome, and this I think was the  
16 working diagnosis for the child's admission to the  
17 Hospital, and for the child's work-up in the Hospital,  
18 and then to call it SIDS, to me doesn't really make  
19 too much sense.

20 Q. So you prefer sick sinus  
21 syndrome?

22 A. Yes.

23 Q. As a diagnosis in the absence of  
24 digoxin?

25 A. Right.

Q. How then do you account for the





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CC112 pathological findings on autopsy that are consistent  
3 with SIDS?

4 A. Well, as I said before the  
5 pathological findings are supportive. They are  
6 probably related to some degree to chronic hypoxia  
7 or acute episodes, repeated acute episodes of hypoxia.  
8 I don't think they are specific enough and I think  
9 they help, but they in themselves are not conclusive.

10 Q. I would like to turn to the  
11 cases of Lombardo and Belanger, and I don't think you  
12 need the charts for the questions I am going to ask  
13 you.

14 I take it that these were two of the  
15 babies that were not prescribed digoxin but digoxin  
16 was found in their tissues, and I take it that the  
17 main points of significance for you in looking at  
18 these two babies was, first, the fact that digoxin  
19 was found in their tissues when they were not pre-  
20 scribed digoxin.

21 Secondly, you indicated with respect  
22 to these babies that even though the levels were  
23 found in exhumed or embalmed tissues, they were high  
24 enough to be of some quantitative value to you; is  
25 that correct?

A. I think maybe you had better







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show me because I don't remember the details.

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Q. Lombardo is found at page 52 of your report; and Mr. Cimbura's levels on Lombardo are found in Exhibit 95C, at page 2. Do you have that?

A. I don't have the exhibit, no.

MS. FORSTER: I wonder if the witness can be given Exhibit 95, please.

Exhibit 95C, at page 27.

A. Yes.

Q. The levels that Mr. Cimbura found in the exhumed tissues of Stephanie Lombardo.

A. Yes.

Q. And I believe he indicated that the levels were high enough in this case that you found them to be of some significant value.

A. Do you have the reference to that?





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Q. Not at hand.

Do you find them to be of significant quantitative value?

A. Yes.

Q. Dr. Kauffman in his report deals with the digoxin assays in exhumed and embalmed tissue and I would like to put to you some of the comments he made about digoxin assays in these kinds of tissues and ask you whether you agree or disagree, and I am reading from page 3 of his report:

"Digoxin assays in exhumed, embalmed tissue presents several additional problems. First, digoxin has been shown to be unstable in at least one embalming fluid and undergoes a significant amount of chemical degradation over a period of months. This would have the effect of reducing the apparent concentration of digoxin."

Do you agree with that statement, Doctor?

A. Yes.

Q. "Second, nothing is known about the degree to which digoxin tissue binding is altered by post mortem changes and to what extent the drug





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"re-equilibrates in post mortem  
tissues."

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Do you agree with that as well?

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A. Would you read this again?

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Q. Yes.

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THE COMMISSIONER: Equilibrates,  
I think is the word.

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MS. FORSTER: Yes.

9

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Q. "Second, nothing is known about  
the degree to which digoxin tissue  
binding is altered by post mortem  
changes and to what extent the drug  
re-equilibrates in post mortem  
tissues."

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A. Yes.

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Q. "Third, desiccation of the  
tissues occurs to varying degrees  
with time depending upon burial  
conditions and may potentially result  
in erroneously high apparent  
concentrations of digoxin."

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Do you agree with that?

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A. Yes.

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Q. And then he says:

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"These uncontrolled and unmeasurable

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"variables make it virtually impossible to quantitatively interpret digoxin concentrations in exhumed tissues. Therefore, as with the preserved tissues, the usefulness of these assays is essentially limited to documenting the presence or absence of digoxin. Alone they do not necessarily indicate digoxin toxicity."

Do you agree with that statement, Doctor?

A. Not completely.

I stated yesterday on several occasions that I think I would be very hesitant to attribute any quantitative value to these measurements except perhaps in situations such as these where here you have a baby that was not prescribed any digoxin and yet the levels are high. Very high.

Now I don't think anybody has a lot of experience on exhumed bodies and to know what exactly happens, and I think one has to be very, very cautious and very conservative in expressing an opinion.

But I don't see how, for instance, if







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this child had been given an accidental dose,  
maintenance dose or - unless it was a very high dose,  
like a digitalizing dose - that such level would  
occur.

No matter how you look at it to obtain  
such high levels would take, you know, a certain  
amount of digoxin in the body and it would be very,  
very difficult to explain this as perhaps a small  
error of giving a maintenance dose of the drug to  
somebody who was not supposed to receive it.

Q Well, other than the cases that  
you have dealt with in your report have you had any  
experience interpreting digoxin levels in exhumed or  
embalmed tissue, Doctor?

A. You mean other than the cases  
in this --

Q Yes?

A. No.

Q Are you aware of any literature  
on the subject?

A. I am aware of some very recent  
literature. I can't give you the references offhand,  
but there are - there is some very recent literature  
of isolated incidences, but I don't think that there  
is a lot of experience in general with exhumed bodies





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and the concentration of digoxin.

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Q Does this literature that you have referred to deal with the levels one might expect to find in exhumed or embalmed tissue after therapeutic or toxic administration of digoxin?

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A To my recollection they were within the usual range that one would expect therapeutically or perhaps slightly higher, but these were individuals who had received it.

10

11

Q Do you recall how long the bodies covered in this article had been buried?

12

A I don't remember the details.

13

Q All right.

14

A I would have to look it up.

15

Q I just had one other question for you, Doctor.

16

17

18

You mentioned that it was possible for a person who was given an overdose of digoxin to die before the digoxin had its peak effect? Correct?

19

A Yes.

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Q Is it also possible for someone to die after the peak effect is over?

21

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A Yes, it is possible.

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The myocardium becomes very sensitized once the peak effect is reached, and even though the





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concentration may be slowly coming down with time  
it is a very slow process.

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It takes 30 hours or 36 hours for it  
to become half of what it was originally.

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The myocardium is still very sensitive  
during this entire period of time, and any other  
insult, for instance fever, whatever, medication  
perhaps, could precipitate an arrhythmia or produce  
an arrhythmia which could be fatal then.

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MS. FORSTER: All right. Thank you.

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THE COMMISSIONER: Thank you, Miss Forster.

Miss McIntyre, what do you think your chances are of completing within 15 minutes?

MS. MCINTYRE: I think they should be quite good, particularly since I am not available on Monday.

THE COMMISSIONER: All right.

MS. MCINTYRE: That puts a certain pressure on me too.

THE COMMISSIONER: I would like to express it another way: If you don't finish within 15 minutes you will have to be available on Monday.

MS. MCINTYRE: Yes, I appreciate that.

CROSS-EXAMINATION BY MS. MCINTYRE:

Q. Dr. Hastreiter, my name is Elizabeth McIntyre and I appear on behalf of the Registered Nurses Association of Ontario and 39 individual nurse.

I know you have been referred at several times already today, but I have yet a few more questions about your case report, Exhibit 276.

THE COMMISSIONER: I am sorry, 2?

MS. MCINTYRE: 276, the overdose







1  
2 incident.

3 Q. And I would direct your  
4 attention to page 485, the last paragraph before  
5 the conclusion where you have referred to - you  
6 were dealing with a single overdose in this instance  
7 that you have referred to reports of 5 additional  
8 infants who died following accidental massive  
9 overdose of intravenous digoxin, and you have set  
10 the details of those out on the next page in a  
11 table.

12 I take it, Doctor, that these would  
13 all have occurred in a hospital setting like the  
14 one your were dealing with?

15 A. These are reports from the  
16 literature, yes, they occurred in hospitals.

17 Q. I gather that from the  
18 fact they are intravenous they would have to be  
19 in a hospital setting?

20 A. That is right.

21 Q. I am interested in the  
22 particulars that are set out in Table 2 which appears  
23 on page 486 where there seems to be considerable  
24 variation in the various factors that are listed.

25 What I found of particular interest  
was the interval reported from dose to death, which

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in three of the cases, the second, third and fifth, appear to be quite long. That is 8 hours, 6 hours and 5.5 hours.

Would you not agree with me that those would all be after steady state was reached?

A. Yes.

Q. Most likely?

A. Yes.

Q. Or to put it another way after the peak effect had been reached?

A. Yes.

Q. Of the digoxin?

A. Yes. This disturbed me a little bit too when I read these reports, and unfortunately that is the situation, you know.

I wondered about these figures whether these numbers are correct times and all that, because these are usually reports - for instance, Seletzky's -

Q. That is the last one?

A. Yes, forensic pathologist reports, so there was not clinical information practically available. And Phillip's I think there was a little bit of clinical information but there was really not a great deal, and these reports are generally not very good.





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So I take it that the information is limited but it would tend to indicate that even where there is death from digoxin overdose the period of time between administration and death can be quite substantial?

A. Yes, it would appear that way.

Q. And particularly in the last case it would appear that the dose administered was a large dose, even larger than the one that you dealt with in your particular case study, being 3 milligrams, which I take it is the equivalent of 6 adult ampoules of digoxin?

A. Yes. It is almost unbelievable.

Q. But it is reported as an error in administration?

A. Yes.

Q. And I take it that would be --

THE COMMISSIONER: I take it these all have to be hospital errors. They aren't - I suppose you can't expect a three day old child to be taking - I guess none of these children ...

THE WITNESS: These are all --

THE COMMISSIONER: It may have been on something at home but it wasn't --

MS. McINTYRE: Mr. Commissioner, it





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does in the text it says that they are all intravenous  
injections.

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THE COMMISSIONER: Oh, yes, I beg  
your pardon. You are quite right.

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THE WITNESS: These are all intravenous.

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THE COMMISSIONER: Yes.

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THE WITNESS: There are several cases  
of oral administration of digoxin that also led to  
death which are not included here. These were usually  
older children and not in this age range.

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THE COMMISSIONER: Do they say how  
they were administered intravenously because, you see,  
if they were put high - as I understand it the higher  
up on the intravenous apparatus they are put the  
longer it will take to get into the child?

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THE WITNESS: That is true.

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THE COMMISSIONER: And if they don't  
give us that, then the time interval doesn't mean  
anything.

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THE WITNESS: I don't believe that  
these details are available, but perhaps we should  
really look at the description of these cases in  
a little more detail if we can get them.

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MS. McINTYRE: Q I take it that the  
reports could be found in a medical library?

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A. Oh, yes, very easily.

Q. Now, Dr. Hastreiter, I want to take you back to the case of Justin Cook once again.

A. Yes.

Q. With respect to the evidence you gave on your estimated time of administration which you told Mr. Lamek was between 3:15 and 3:40 in your opinion. That is at Volume 75, page 6610.

I was a little confused as to whether or not you based that on the level of digoxin that was found in the myocardial tissue or on the first clinical evidence of possible toxic effects?

A. I think it is a combination of factors really.

First of all, the fact that with an intravenous bolus of digoxin usually the initial effect will occur from 5 to 30 minutes following the administration, so we were looking at the child's symptoms at 3:45. They occurred at 3:45.

If you go back 5 to 30 minutes it will be the appropriate time.

Q. So that is where the 3:15 came from?

A. That is where the 3:15 came from. But in addition you have to more or less try and match





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Hastreiter, cr.ex.  
(McIntyre)

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this timing with the high level found in myocardium,  
and in blood. The blood was drawn at 4:30 I believe  
and the myocardium was of course after death which  
occurred at 4:56.





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Q Yes, Okay. So, it is a combination of the two things, of those two factors?

A Yes, two or three factors.

Q And I take it this morning that you also introduced the element when you were talking to Mr. Brown you said that you assumed that the death or that the administration could not have been too long before death in that you did not think the child could have survived with such high levels for a very long period of time?

A Yes, I believe I said that.

Q Okay. Now, dealing with those three items, I take it that if in fact the information that you have provided in this table, in Exhibit 276 is correct, that that would indicate that a child could in fact survive for quite a long period of time even after being given a very substantial dose; in particular the last reference to the Seletsky case where there was a dose of 3 milligrams and there was a 5.5-hour interval?

A Well, you know, I think one has to be very cautious about looking at case reports from the literature. I really feel that perhaps what we should do is look at these reports again because I remember very well in Seletsky's report there were





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several errors in the numbers, figures, and I had difficulty figuring out what the true numbers really were, and perhaps this would be the best thing to do because if you place a lot of reliance upon this information and it turns out not to be very good I think you will be really wrong.

Q. Well, I take it that what you were putting forward this morning was your own theoretical understanding that a child could not survive for a long period of time with a high level in the blood?

A. That is correct.

Q. That is not based on any empirical information?

A. No. Of course, it is almost impossible to produce a situation where you can monitor a child with a very high blood level for a long period of time, but I think in general, if you look at the literature, in situations where the blood level, pre mortem I'm talking about now, was higher than 20 nanograms per ml, the prognosis is very bad. Cases where the highest level was below 20, there have been survivors and especially nowadays with modern treatment, with antibodies, FAB fragments, there have been survivors and in fact there has been







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one survivor whose level was higher than 100, but  
this child was very, very sick, having all kinds of  
arrhythmias and was given the antibodies and the  
level immediately fell very rapidly and the child  
eventually was all right.

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Q Would it be fair to say then  
that the empirical data that is available is not  
conclusive in terms of ability to survive with, or  
length of survival given in overdose?





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A. Well, I think that we can very definitely state that there are no data available on length of survival with extremely high blood levels such as 70 or 100 which we encountered here.

There is a great deal of information available about high levels and whether or not they produce death or not and I think some inferences or some conclusions are drawn from the clinical course, or from the response to treatment and so forth of these children. There are a number of instances of individuals who were poisoned with digoxin whose blood levels were drawn sequentially, but those were usually the ones who survived, because if you could draw them sequentially for several hours they must have been alive and it was usually coming down and they eventually survived.

So, in answer to your question, no, there are no data available.

Q. Well, perhaps over the weekend we can get the individual cases to which you have referred and see if they would be of any further assistance.

A. Yes.

MS. McINTYRE: Mr. Commissioner, it would appear that I am either going to have to end





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here or else make myself available on Monday.

THE COMMISSIONER: I take it you are ending there then, is that it?

MS. McINTYRE: I will do my best, thank you.

THE COMMISSIONER: I am sorry, I don't know what your best is.

MS. McINTYRE: Well, I may come back on Monday if I can dispose of my other obligation.

THE COMMISSIONER: Yes, all right.

MR. BROWN: Sir, if I may briefly raise a matter for your consideration and for fuller argument at a later date.

THE COMMISSIONER: Yes.

MR. BROWN: A number of counsel have reviewed the Reasons of Judgment that you released in respect of the baby names.

THE COMMISSIONER: Yes.

MR. BROWN: And in respect of the notice question and counsel for Nurse Nelles, Nurse Trayner, for Registered Nursing Assistant Brownless, Christie and The Registered Nursing Assistants Association of Ontario are requesting of you to state a case to the Divisional Court with respect of those two matters.





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THE COMMISSIONER: Which two matters,  
I'm sorry?

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MR. BROWN: In respect of the naming  
names and in respect of compliance with Section 5(2)  
of The Public Inquiries Act.

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Mr. Olah is joining our application  
in respect of the naming names. I understand --

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MR. SHANAHAN: I can't hear Mr. Brown.  
The last thing I heard was Mr. Olah.

MR. BROWN: Mr. Olah is joining our  
application in respect of naming names and I understand  
he has a separate application in respect of the  
compliance with the statute.

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THE COMMISSIONER: Yes.

MR. BROWN: If I might, sir, at this  
time simply submit to you for your consideration the  
written request to state the case and that the matter  
be argued in more detail on Monday morning.

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THE COMMISSIONER: Do you mean it  
seriously Monday morning?

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MR. BROWN: At the most convenient  
break in the proceedings.

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THE COMMISSIONER: Well, I mean, have  
you given some thought to it, are people available  
on Monday morning?







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MR. BROWN: To my understanding the parties who are joining the application are.

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THE COMMISSIONER: Was that what all that activity was about?

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MR. BROWN: Yes, I apologize.

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MR. OLAH: Mr. Commissioner, my client is in a somewhat different position with respect to the issue of notice and consequently we felt that it is imperative that a separate stated case be brought with respect to her. I have a copy of the stated case for consideration. Of course, if you find it incomplete or, for that matter not as comprehensive as you would like, we would be delighted to amend it.

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THE COMMISSIONER: Yes. Well, I don't want to give away any secrets but I don't think you will find any trouble with me on the first question; you will have to do some heavy persuasion on the second. But even if you don't like what I do, you know, you have your remedy.

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If it is going to be argued at 10:30, it will have to be, because I am in the Court of Appeal briefly on Monday morning, at 10:30, there is no reason to have Dr. Hastreiter back for that morning. How long do you intend to be?





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MR. BROWN: I don't intend to be very long.

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THE COMMISSIONER: But there may be other counsel of course who may be opposed.

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MR. BROWN: That may very well be.

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THE COMMISSIONER: And if they are - is everybody getting a copy of this document?

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MR. BROWN: I will give them copies, sir.

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THE COMMISSIONER: Yes, all right.

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MR. OLAH: I have a copy of our stated case for them.

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THE COMMISSIONER: Yes, do you have copies for everybody?

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MR. OLAH: Yes, I do, sir.

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THE COMMISSIONER: All right. Well, I will take those. What are your plans, Dr. Hastreiter? I suppose you would like to become a doctor again?

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THE WITNESS: Yes.

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THE COMMISSIONER: Instead of a professional witness?

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THE WITNESS: Yes.

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THE COMMISSIONER: But you will be here on Monday morning in any event?

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THE WITNESS: Yes.





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THE COMMISSIONER: You will in any event?

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THE WITNESS: Yes.

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THE COMMISSIONER: Because it is conceivable we will only be about an hour on this matter, in which case if you are here we will continue at 11:30; if on the other hand you are taking a flight in on Monday morning you could take a later one or something like that.

MR. LAMEK: Mr. Commissioner, may I suggest something please?

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THE COMMISSIONER: Yes.

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MR. LAMEK: As you know, and I think perhaps now everybody knows through informal notice Dr. Mirkin will not be here before Christmas.

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THE COMMISSIONER: Yes.

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MR. LAMEK: And it is entirely likely that in the latter part of next week frankly we may run a bit short of evidence. Rather than hold up Dr. Hastreiter and imperil his departure, can we not deal with him as soon as we can on Monday morning? I can't conceive that there is so much urgency about the stated case application that it couldn't be heard on perhaps Wednesday of the week. It is not going to be argued before the New Year anyway in the





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Divisional Court even if you state the case.

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MR. BROWN: I think Mr. Lamek's

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suggestion is very convenient to the witness and if he doesn't anticipate any witness, then we can do it that way.

THE COMMISSIONER: All right. Well, let's proceed at 10:30 then with the evidence and I will keep this thing close to my heart or bosom or something until Wednesday and then we will deal with it on Wednesday and if Dr. Hastreiter is still giving evidence it will be when he is finished.

MR. BROWN: Fine.

THE COMMISSIONER: Otherwise it will be Wednesday at 10:30 then because I have another matter on Wednesday.

All right?

MR. BROWN: Thank you, sir.

THE COMMISSIONER: So, until 10:30 on Monday.

--- Whereupon the Hearing adjourned at 3:45 p.m. to be reconvened at 10:30 a.m., Monday, December 12th, 1983.







